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I. THE REACTION TO POSTERIOR PITUITARY EXTRACT (PITUITRIN) WHEN INTRODUCED INTO THE CEREBRAL VENTRICLES*

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Introduction.—In 1908,[1] P. T. Herring first clearly described the peculiar hyaline bodies often seen in sections of the neuro-hypophysis and expressed the belief that they represented the secretory product of the epithelial investment of the posterior lobe known as the pars intermedia. The globules appeared to find their way toward the tuber cinereum and in favorable histological preparations could be seen passing between the bodies of the ependymal cells to enter the infundibular cavity.

Two years later (1910), Cushing and Goetsch,[2] in support of Herring's postulation, supplied experimental evidence in two directions: (1) by showing how occlusion of the pituitary stalk served to dam back the secretory product in the pars nervosa; and (2) by demonstrating, however inconclusively, that the active principle of the lobe was detectable in the cerebrospinal fluid, their deductions having been based on the haemodynamic, peristaltic and diuretic responses to concentrated human ventricular fluids injected for the most part intravenously into rabbits.

From *the histological side* Herring's discovery has received abundant substantiation, though interpretations regarding the source of origin and destination of the hyaline bodies have varied. It is evident that the cells of the pars intermedia et tuberalis, under some nervous stimulus, disgorge their ripened cytoplasm into the pars nervosa and that the extruded product undergoes hyalinoid transformation during its migration upward, toward and into the tuberal projection of the diencephalon. Indeed,

* Although the attention of physiologists and pharmacologists was first called to the pituitary body by the discovery of the haemodynamic and diuretic properties found in extracts of its posterior lobe, the function of this obviously important portion of the gland has remained a physiological mystery. One of my anatomist friends who has made notable contributions to our knowledge of the anterior lobe hormones has challenged me to produce any corresponding clinical or experimental evidence of posterior lobe activity. To this challenge this and the succeeding papers are a partial answer.

under certain circumstances large numbers of apparently intact cells, for they still contain recognizable nuclei, may actually thus migrate from its epithelial investment into the substance of the pars nervosa in their passage through which they subsequently become hyalinized.*

This casting off of the cytoplasm in mass or actual discharge of the entire cell body are by no means unique modes of secretion of glandular cells.** What is more, the process, as we know now, is unquestionably under the direct control of certain nerve centers in the interbrain. The presence of a large number of non-myelinated nerve fibers in the neurohypophysis, apparently first observed by Ramon y Cajal in immature mice (1894), was subsequently confirmed by his pupil, Tello[3] (1912), for the human gland. It, however, was not until the papers of Pines[4] (1925) and of Greving[5] (1926) that the diencephalic centers, from which the fibres take their origin, and their amazingly rich arborization in the posterior lobe came to be fully appreciated and was brought to the attention of physiologists and clinicians.

The interstitial passage of the hyaline bodies through the neurohypophysis and its stalk toward the tuber has meanwhile been observed by many. Edinger[6] injected the posterior lobe with india-ink and though the mass tended to spread in the direction of the tuber, it did not enter the ventricle. Herring, however, as did Cushing and Goetsch, gave photomicrographs showing hyaline globules actually caught in the process of their extrusion into the ventricle, an observation which has been confirmed among others by Hines,[7] by da Costa,[8] by Espino,[9] and by Remy Collin.[10,11,12]

From *the physiological side*, though the conclusions drawn from their early experiments by Cushing and Goetsch met with criticism,[13] the unmistakable presence in the fluid of a substance, which if not the active principle at least possesses similar properties, has since been clearly demonstrated by a number of workers who have taken advantage of the more exact and dependable oxytocic and melanophore-expanding properties of the extract subsequently discovered by Dale and by Hogben. Thus Cow[14] (1915), Dixon[15] (1923), Trendelenburg[16] (1924), Jánossy and Horváth[17] (1925), Miura[18] (1925), Trendelenburg[16] (1926), Blau and Hancher[19] (1926), Mestrezat and v. Caulaert[20] (1926), McLean[21] (1928), Hoff and Wermer[22] (1928), and Karplus and Peczenik[23] (1930), have

* A photomicrograph illustrating such a cellular migration was given in the author's monograph on the pituitary body, 1912, page 199.

** The three methods of secretory discharge which histologists now recognize are: (1) *merocrine*, in which the secretory granules are periodically extruded without particular change of form in the cell, as in salivary, gastric or anterior pituitary glands; (2) *holocrine*, in which the entire cell body is cast off, as in the sebaceous glands; (3) *apocrine*, in which the ripened cytoplasm is disgorged, as in mammary secretion and in the case of certain cutaneous glands, particularly of the lower animals.

successively shown: (1) that a substance, whose pharmacological properties resemble those of posterior lobe extract,* is often demonstrable in normal ventricular and cisternal though not in the lumbar fluids;[20] (2) that it may be augmented by the administration of certain organic extracts[15] as well as by certain drugs particularly those producing diuresis;[22] (3) that it disappears after hypophysectomy or occlusion of the pituitary stalk;[16] (4) that it is increased by emotional stimuli;[22] and finally (5) that it is augmented by direct electrical stimulation of the hypothalamus or tuber.[23]

McLean[21] in the writer's laboratory was led to believe that the active principle is detectable in the jugular vein in larger amounts than in the cerebrospinal fluid. He consequently concluded that it was initially absorbed solely by the vascular route (the abundant "portal circulation" connecting hypophysis and hypothalamus recently described by Popa and Fielding[24] would readily make this possible), and that, being a readily dialysable substance, it found its way into the cerebrospinal fluid through the choroid plexuses. On the other hand, the recent brilliant demonstration of Karplus and Peczenik,[23] who showed that the amount of the oxytocic and melanophore-expanding substance in the fluid is increased by electrical stimulation of the tuber, amply justifies their conservative conclusion that the active principle of the posterior lobe is discharged, at least in part, into the ventricular fluid.

It was the original assumption of Goetsch and Cushing that the extrusion of the hyaline bodies between the ependymal cells into the infundibular cavity, whence they were swept along by the cilia of the ependymal cells until dissolved, represented a form of "external secretion" which, in its cerebrospinal fluid medium, was destined ultimately to reach the blood stream by way of the arachnoid villi. It did not occur to them that the substance owing to its ready diffusability might, by resorption, act directly upon subependymal nerve centers in the walls of the third ventricle. Indeed, twenty years ago little was known of these hypothalamic nerve centers, and the functional importance of the diencephalon was scarcely suspected.

Intravenous Versus Intraventricular Effects of Pituitrin.—When injected intramuscularly or intravenously, in addition to its well-known antidiuretic effect pituitrin causes prompt blanching of the skin and mucous membranes from a vigorous vaso-constrictor action, dryness of the mouth

* It should be mentioned that Van Dyke, Bailey and Bucy (*J. Pharmacol. & Exper. Therap.*, 1929, **36**, 595–610) after a painstaking chemical study have come to the conclusion that the oxytocic and melanophore-expanding effects of cerebrospinal fluids are wholly ascribable to differences in the calcium concentration between the test fluids and the bathing fluids. They have made a strong case but it would be difficult to believe, for example, that an increase in the oxytocic and melanophore-expanding properties of the fluid after electrical stimulation of the tuber could be due to increase of calcium.

from loss of salivary secretion, and an early evacuation due to stimulation of the lower bowel. That injection of the extract directly into the cerebral ventricles calls forth a wholly different response was briefly reported in a recent address dealing in general with what were called neurohypophysial mechanisms.[25] It was there stated that the extract thus injected will in certain cases cause an astonishingly prompt response characterized by intense flushing from vaso-dilatation, by profuse perspiration, by retching and vomiting, by salivation, by a marked fall in body temperature, and by a coincidental lowering of the basal metabolic rate. These responses occur in the absence of any significant pupillary change, pilomotor reaction, or stimulation of the lower bowel.

Though the intensity of the reaction varies considerably from case to case, the following protocol may serve as an illustration of a moderately pronounced effect:

The patient, a vigorous young man with outspoken acromegalic gigantism, was admitted to the hospital on December 8, 1930, with the single complaint of failing vision. He was found to have a bitemporal hemianopsia with primary optic atrophy and loss of reading vision with a greatly expanded sella turcica.

On December 19th the usual right transfrontal osteoplastic exploration was made. A large chromophile adenoma was exposed and radically excavated by a combination of electro-surgical methods and suction, restoration of the temporal fields of vision being demonstrable at the conclusion of operation. He made a perfect recovery from this procedure with no polyuria or other evidence of tuberal contusion.

Apart from the prompt restoration in vision, the only postoperative change detected was a considerable drop (20 points) in the basal metabolic rate, together with the customary loss in weight shown by acromegalics after one of these operations. He was a coöperative and intelligent young man and before his discharge willingly submitted to the tests which we proposed to make.

8.30 A.M. January 8, 1931. Preliminary Observations.—Fasting. Basal metabolic rate −13. Weight 85.8 kgm. Erythrocytes 5,160,000. Blood sugar 0.099. Voided 440 c. cm. urine. Rectal temperature 99.8°F.* Pulse 80. Room temperature 73°F. Respiration 21. Blood-pressure 130/80. Skin dry. Hands and feet rather cool and moist. Pupillary measurements registered.

10.39 A.M.—Injection into lateral ventricle of 1 c. cm. of "surgical pituitrin."

10.45.—Sensation of warmth. Definite flushing of skin except over site of bone flap. Sudden profuse sweating.

10.51.—Slight fall in blood-pressure. Profuse perspiration with no appreciable lachrymation, salivation or change in pulse. Complaint of intestinal uneasiness. Borborygmi auscultable. Hands and feet have become warm.

10.58.—Flushing has become very pronounced. Sweat excessive. Pillow and sheets wringing wet (cf. frontispiece).

11.00.—Temperature beginning to fall. Erythrocytes 4,550,000. Blood sugar 0.121. No pupillary change.

11.11.—Rectal temperature 99.3°. Flush persists. Slight temporary increase in pulse rate to 100. Brief preliminary drop in systolic blood-pressure to 110 now followed by pressor response to 140.

* In all these observations the continuous record of the rectal temperature has been taken on a Leeds & Northrup Resistance Thermometer Recorder.

11.20.—Temperature falling rapidly. Now 98.5°. Flush persists. Perspiration still excessive. Nauseated but no cramps.

11.30.—Rectal temperature 97.7°. Condition otherwise unchanged.

11.38.—Gradual slowing of pulse to 60 and of respiration to 12. Blood-pressure fallen to pre-injection level of 130. Rectal temperature 96.8°.

11.50.—Rectal temperature 96°. Flush fading. Perspiration much diminished.

12.00 Noon.—Rectal temperature 95.3°. Flush barely perceptible. Skin drying. Still nauseated.

12.10 P.M.—Rectal temperature 94.8°. Pulse 60.

12.20.—Rectal temperature 94.2°. Vomited 75 c. cm. of bile-stained mucous fluid.

12.30.—Rectal temperature continues at 94.2°, its lowest point, a drop of 5.6° F. in 1 hour 40 minutes. Erythrocytes 4,800,000. Blood sugar 0.114.

12.41.—Basal metabolic rate −31. Rectal temperature has started to rise, 94.4°. Beginning to feel cold though he has been well covered and room temperature at this time is 77°F.

2.30.—Weight 83.9 kgm. Loss of 1.9 kgm.

2.45.—Vomiting again, 150 c. cm. of yellow mucous fluid. Unable to void voluntarily. Bladder feels empty.

3.00 et seq.—Returned to ward. Rectal temperature (taken by thermometer) did not regain pre-injection level until 6 P.M. and continued to rise to a maximum of 101°F. at 2 A.M. Voided 400 c. cm. at 6 A.M. Morning rectal temperature 99.8°F. 8.30 A.M. basal metabolic rate −1, a rise of 30 points from low injection level of day before.

To summarize: The injection in this case gave a marked reaction, its more striking features being the vaso-dilatation and sweating (sparing the skin over the bone flap); the drop of 5.6°F. in body temperature in the course of an hour and a half with coincidental lowering of the basal metabolic rate from −13 to −31. Vomiting was less pronounced and more tardy in appearance than usual but the patient stated that he never vomits easily. The customary salivation and lachrymation were not noted. There was no temporary increase in erythrocytes as has been observed in some other tests though the loss of fluid from sweating would have led one to expect there might be, regardless of any effect in contraction of the spleen.

Similar injections with variable amounts of the extract (one cubic centimeter of surgical pituitrin being the customary dose) have been made up to the present time on 38 occasions in 24 subjects. The majority of the patients who have submitted to the tests were convalescing from operations for pituitary adenoma of one sort or another, the larger number of them with adenomas of chromophobe variety associated with moderate signs of pituitary insufficiency (hypopituitarism). As this clinical state is usually accompanied by more or less pallor and by an extreme dryness of the skin, the flushing and sudorific response have been the more striking. Because the operations on these patients had been conducted for the purpose of restoring vision due to pressure against the chiasm of a large adenoma, this fact implies that the posterior lobe was in all probability thrown out of function by the expanding intrasellar lesion, which might

conceivably have had some bearing on the intensity of the reaction. However, other persons without pituitary adenomas and with normal third ventricles prove to be equally susceptible to the effects of the injection.

As might be expected, due partly to individual idiosyncrasy of the subjects of these tests as well as to the variety of intracranial disorders by which they were victimized, and due partly to possible differences in the activity of the commercial preparation employed, precise standardization of which is difficult, considerable variability in the intensity of the responses has been observed from case to case. In one patient a cubic centimeter of "obstetrical pituitrin" gave no reaction whatsoever. In another, the customary cubic centimeter of "surgical pituitrin" gave only the slightest reaction; but two days later 1.5 c. cm. gave a severe reaction with the usual pronounced flush, sweating, vomiting, salivation and lachrymation with fall in temperature of 5.9°F. within two hours. In this particular instance, shivering accompanied the fall in body temperature and, contrary to the usual rule, there was a rise in the metabolic rate. Ordinarily the rate falls, a drop from −27 per cent to −50 per cent having been observed in one patient with a chromophobe adenoma.

No characteristic pupillary reaction has been detected in any case. Observations on blood sugar, on blood fat, on the erythrocyte count, have not been as yet sufficiently numerous or sufficiently striking to justify an attempt to interpret them. The expected haemodynamic response has in most cases been surprisingly slight and brief or altogether absent even when the reaction has been otherwise marked; when it has occurred there has usually been a slight slowing of the pulse. There has almost always been a temporary oliguria but the effect on the excretion of urine has been obscured by the fact that the tests have been made on fasting patients with considerable loss of fluid from vomiting and sweating.

The injection in all cases has been made into the lateral ventricle and the question naturally arises as to the way in which the extract acts when thus introduced. Two possibilities suggest themselves: (1) Resorption into the blood stream; and (2) the direct stimulation of hypothalamic nuclei by diffusion of the substance through the ependymal lining of the third ventricle. The former is highly improbable not only because of the promptitude of the reaction but for the reason already mentioned, that pituitrin when injected into the blood stream or intramuscularly has a vaso-constrictor effect and causes cutaneous pallor whereas vaso-dilatation with flushing and hyperhidrosis are evoked by its intraventricular injection. Other evidence of a more negative character, which will be reserved for a subsequent paper, speaks in favor of the view that the extract must act as a direct stimulant to subependymal hypothalamic nuclei.

In three patients who have previously shown a marked reaction to

one cubic centimeter of pituitrin in the ventricle, the commercial products of "pitressin" and "pitocin" have subsequently been given in like (1 c. cm.) amounts. A slight reaction to each substance was observed in one instance but nothing comparable to the effect of pituitrin itself. In one patient, indeed, a cubic centimeter of each substance was given coincidentally with no observable effect whatsoever.

Summary.—Though extracts of the neurohypophysis are known to possess pharmacological activity, extirpation of this portion of the gland or its destruction by disease leads to no symptoms that are as yet clinically recognizable. Nevertheless histological evidence has been provided which shows: that the lobe is under control of an abundant non-myelinated nerve supply from the tuber; that the hyaline bodies of Herring probably represent the secretory product; that these bodies not only may pass into the recently discovered sinusoids of the tuber but also into the ventricular cavity. A substance having the properties of posterior lobe extract has been found by many in the cerebrospinal fluid; stimulation of the tuber has been shown to increase its amount; and commercial pituitrin injected into the ventricle has a pronounced stimulatory effect, essentially parasympathetic in character, apparently nuclear in origin, and presumably due to diffusion of the substance through the ependymal lining of the ventricle.

Conclusion.—Though the function of the neurohypophysis has been wholly overshadowed experimentally and clinically by the recent attention drawn on the one hand to the hormones of the anterior lobe and on the other to the centers in the hypothalamus, the striking response to the injection of its active principle into the ventricle not only gives additional evidence in favor of its normal passage into these cavities, but shows that the posterior lobe must play a far more important rôle in neurophysiology than has been heretofore appreciated.

[1] Herring, P. T., "The Histological Appearances of the Mammalian Pituitary Body," *Quart. J. Exptl. Physiol.*, 1908, **1**, 121–159.

[2] Cushing, H., and E. Goetsch, "Concerning the Secretion of the Infundibular Lobe of the Pituitary Body and Its Presence in the Cerebrospinal Fluid," *Am. J. Physiol.*, 1910, **27**, 60–86.

[3] Tello, F., "Algunas observaciones sobre la histologia de la hipófisis humana," *Cajal's Trabajos X* (Madrid), 1912, 145–183.

[4] Pines, I.-L., "Über die Innervation der Hypophysis cerebri," *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1925, **100**, 123–138.

[5] Greving, R., "Beiträge zur Anatomie der Hypophyse und ihrer Funktion. Eine Faserverbindung zwischen Hypophyse und Zwischenhirnbasis (Tr. supraoptico-hypophyseus)," *Deut. Ztschr. f. Nervenheilk.*, 1926, **89**, 179–195.

[6] Edinger, L., "Die Ausführwege der Hypophyse," *Arch. f. micr. Anat.*, 1911, **78**, 496–505.

[7] Hines, M., "The Hyaline Bodies of the Posterior Lobe of the Hypophysis," *Anat. Rec.*, 1923, **25**, 133–4.

[8] Da Costa, A. C., "Sur les images histologiques d'excrétion dans le lobe postérieur de l'hypophyse," *Compt. rend. soc. Biol.*, 1925, **92**[1], 1246–7.

[9] Espino, A. V., "Contribucion al estudio de las relationes entre la hypofisis y los centros diencefalicos," *Thèse de la Faculté de Med.*, Mexico, 1924.

[10] Collin, R., "Sur l'excrétion de produits hypophysaires dans le liquide céphalo-rachidien," *Rev. Franç. d'endocrinol.*, 1926, **4**, 241–252.

[11] ——, *La Neurocrinie Hypophysaire*, Paris, G. Doin et Cie., 1928, 102 pp.

[12] ——, "La voie céphalo-rachidienne d'excretion de la colloide hypophysaire chez le chat," *Arch. d'Anat. microscop.*, 1929, **25**, 69–74.

[13] Carlson, A. J., and L. M. Martin, "Contribution to the Physiology of Lymph. XVII. The Supposed Presence of the Secretion of the Hypophysis in the Cerebro-spinal Fluid," *Am. J. Physiol.*, 1911–12, **29**, 64–75.

[14] Cow, D., "On Pituitary Secretion," *J. Physiol.*, 1914–15, **49**, 367–377.

[15] Dixon, W. E., "Pituitary Secretion," *Ibid.*, 1923, **57**, 129–138.

[16] Trendelenburg, P., "Die Sekretion des Hypophysenhirnterlappens in die Cerebro-spinalflüssigkeit," *Klin. Wochschr.*, 1924, **3**[1], 777–779. Also: "Weitere Versuche über den Gehalt des Liquor cerebrospinalis an wirksamen Substanzen des Hypophysen-hinterlappens," *Arch. exptl. Path. Pharmakol.*, 1926, **114**, 255–261.

[17] Jánossy, J., and B. Horváth, "Nachweis des Hypophysensekretes im Liquor der menschlichen Cisterna cerebello-medullaris," *Klin. Wochschr.*, 1925, **4**[2], 2397–9.

[18] Miura, Y., "Über den Gehalt der Cerebrospinalflüssigkeit an Hypophysenhinter-lappensekret," *Arch. ges. Physiol.*, 1925, **207**, 76–84.

[19] Blau, N. F., and K. G. Hancher, "The Uterine Contracting Power of the Spinal Fluid after the Administration of Extracts from the Sex Glands and Other Organs," *Am. J. Physiol.*, 1926, **77**, 8–23.

[20] Mestrezat, W., and van Caulaert, "Présence de la sécrétion hypophysaire dans le liquide céphalorachidien ventriculaire et dans les liquides de ponction haute," *Compt. rend. soc. Biol.*, 1926, **95**[2], 523–525.

[21] McLean, A. J., "The Route of Absorption of the Active Principles of the Posterior Hypophysial Lobe," *Endocrinology*, 1928, **12**, 467–490.

[22] Hoff, H., and P. Wermer, "V. Untersuchungen über die Sekretion des Pituitrins unter dem Einfluss harntreibender Mittel. VI. Über psychische Beeinflussung der Tätigkeit des Hypophysenhinterlappens," *Arch. exptl. Path. Pharmakol.*,192 8, **133**, 84–102.

[23] Karplus, I. P., and O. Peczenik, "Über die Beeinflussung der Hypophysentätigkeit durch die Erregung des Hypothalamus," *Arch. ges. Physiol.*, 1930, **225**, 654–668.

[24] Popa, G., and U. Fielding, "The Vascular Link between the Pituitary and the Hypothalamus," *Lancet* (Lond.), 1930, **2**, 238–240.

[25] Cushing, H., "Neurohypophysial Mechanisms from a Clinical Standpoint," *Lancet* (Lond.), 1930, **2**, 119–127, 175–184.

II. THE SIMILARITY IN THE RESPONSE TO POSTERIOR LOBE EXTRACT (PITUITRIN) AND TO PILOCARPINE WHEN INJECTED INTO THE CEREBRAL VENTRICLES

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In the preceding paper it was pointed out that the intraventricular injection of "pituitrin" has a profoundly different effect from that which follows its subcutaneous or intravenous administration. Instead of the customary pallor of the skin with evacuation of the bowels, there usually occurs a prompt cutaneous vaso-dilatation with an extreme sudorific effect, often with repeated vomiting and a considerable fall in body temperature.

This peculiar and striking response to pituitrin when put in the ventricles was so suggestive of the known pharmacological reaction to pilocarpine that it seemed advisable to make comparative studies of the effect of the extract and of this drug. Accordingly, in one of the patients who had shown at an earlier session a well-marked reaction to intraventricular pituitrin a test was first made with a subcutaneous injection of 12 mgm. of pilocarpine. This led to the familiar response characterized by moderate flushing, slight sweating with salivation and lachrymation, some intra-abdominal uneasiness but no vomiting, a temporary increase of 20 points in the pulse rate but no change in blood-pressure or pupils, and an insignificant fall in rectal temperature of 0.8°F. A slight rise of 7 points in the basal metabolic rate was observed but this was considered to lie within the margin of error.

On the following day, less than half of this dose of pilocarpine, namely, 5 mgm., was introduced into the lateral ventricle. Almost immediately there was a rise in pulse rate of 20 points without appreciable alteration in blood-pressure or change in size of the pupils. In a few moments the patient had a sensation of warmth soon followed by a marked generalized flush, a drenching perspiration and excessive salivation accompanied by prolonged retching and vomiting. In the course of the next two hours the temperature dropped off two degrees, from 98.8° to 96.8° but with no change in the basal metabolic rate.

This reaction was more severe than had been anticipated and in the six other patients, on whom similar tests have subsequently been made, one-half of this amount of pilocarpine, namely, 2.5 mgm., has been introduced; but this smaller dose has elicited the same prompt and striking reactions in all instances but one. The exception was in a patient who had a glioma involving the tuber and in whom the intraventricular injection of one cubic centimeter of surgical pituitrin had likewise caused no appreciable effect.

To show how nearly comparable are the reactions to the two substances administered in this way the following protocols may be given side by side.

The patient, John S., was convalescing from an operation for the removal of a large glioma of the left temporo-occipital region unassociated with hydrocephalus. At the time the tests were made his wound was healed, there was no tension and he was wholly free from symptoms. A previous intraventricular injection of 1 c. cm. of surgical pituitrin in the ventricle had caused a definite though inconspicuous response leading to a fall of temperature of one degree only and, contrary to the usual rule, a rise in metabolism from +1 to +8. He was then given a test with 2.5 mgm. of pilocarpine which evoked such a marked reaction that on a subsequent occasion, for better comparison of the two effects, a dose of 1.5 c. cm. of pituitrin was injected. The protocols of these two injections are subjoined.

Reaction to Pilocarpine (Cf. Chart I)	Reaction to Pituitrin (Cf. Chart II)
Jan. 17, 1931. Preliminaries, 9 A.M. *et seq.* Basal metabolic rate −1; weight 65.4 kgm. *Blood:* erythrocytes 5,010,000; sugar 0.124 mgm.; total lipoids 0.652. Pupils 5 mm. (unaffected throughout). Rectal temp. 99°F.; pulse 65; blood-pressure 124/75.	*Jan. 22, 1931.* Preliminaries, 9 A.M. *et seq.* Basal metabolic rate, +3; weight 66.4 kgm. *Blood:* erythrocytes 4,290,000; sugar 0.098 mgm.; total lipoids 0.635. Pupils 4.5 mm. (unchanged throughout). Rectal temp. 98.9°F.; pulse 65; blood-pressure 124/76.
10:30 Ventricular tap; 5 c. cm. fluid withdrawn.	10:28 Ventricular tap; 5 c. cm. fluid collected.
10:38 *Injection 2.5 mgm. pilocarpine* with prompt slight enduring rise in blood-pressure to 156/95.	10:38 *Injection 1.5 c. cm. surgical pituitrin* with prompt slight enduring rise in blood-pressure to 150/90.
10:43 Borborygmi; nausea; vomiting; slight flush.	10:42 Nausea; slight flush; feels warm; skin moist.
10:48 Continued vomiting; marked flush; free sweat.	10:47 Perspiring freely; salivation; lachrymation; blood for erythrocytes 4,570,000.
11:09 Periodical retching and vomiting continuous. Heavy sweat.	11:00 Marked flush; heavy sweat; nausea continues.
11:10 Temp. begins to drop (32 minutes).	11:04 Temp. begins to drop (26 minutes).
11:17 Retching; vomitus blood-streaked.	11:31 Continued rapid fall in temp. to 96.4°; no vomiting.
11:20 Blood: erythrocytes 4,950,000; sugar 0.160; total lipoids 0.685.	11:47 *Blood:* erythrocytes 4,450,000; sugar 0.111; total lipoids 0.657.
11:30 Sweat still profuse; retching less frequent.	12:10 Flush fading; cessation of sweat; temp. 93.8°.

REACTION TO PILOCARPINE (CF. CHART I) (*Continued*)

12:20 Flush fading; skin drying; temp. 96.6°.

12:35 Reaction practically over. Temperature at lowest level, 96.4°.

1:00 Metabolism taken, +6, Weight 63.8 kgm.

1:20 Chart discontinued. Temp. at 97.2°. Blood-pressure remains slightly elevated. Rectal temperature subsequently taken half-hourly by thermometer; pre-injection temperature not regained until 3:30.

REACTION TO PITUITRIN (CF. CHART II) (*Continued*)

12:29 Reaction about over. Temp. at lowest level, 93°. Shivering though body and extremities warm to touch.

1:00 Metabolism +46 (shivering); weight 64.3 kgm.

1:20 Metabolism +23. Temp. 94°. Comfortable; no shivering.

2:20 Blood; total lipoids 0.686; metabolism +22; temp. 95°.

3:20 Metabolism +26. Temp. 97°.

4:20 Metabolism +29. Temp. 97.8°. Weight 64.3 kgm. Chart discontinued. Subsequent rectal temperatures taken with thermometer half-hourly. Pre-injection temp. of 99° not regained until 7 P.M.

The *similarities* in the reactions to the given doses of pilocarpine and pituitrin noted in these protocols are possibly still more apparent from the plotted records which are here appended (Charts I and II). These charts show the prompt slight pressor response which endured throughout the period of reaction; the secondary slight slowing of pulse rate; and the downward chute in rectal temperature which began after the lapse of about half an hour. Both substances produced the same pronounced flush and drenching sweat which lasted approximately one hour and a half. There was no appreciable change in the size of the pupils with either injection.

The chief *differences* in the responses lay: (1) in the more marked vagal effect from pilocarpine with continued retching and vomiting until positive blood was shown by the guiac test whereas there was only a brief period of nausea with pituitrin; (2) in the far more pronounced and enduring fall in body temperature from pituitrin which persisted long after the cessation of the sweat, the normal rectal temperature not having been regained after the 2.6° drop due to pilocarpine until three hours had elapsed, and after the pituitrin test, with a 5.9° drop to its lowest level of 93°, not until the lapse of six and one-half hours.

One peculiarity in the reactions shown by this patient was the unexpected increase of 43 per cent in the basal metabolic rate which coincided with the lowest temperature caused by the pituitrin injection. For this astonishing reaction with the body temperature at 93° there is

no ready explanation unless it was that the patient was shivering. The finding was so contrary to the usual rule, it was repeated hourly for the next four hours, the rate as recorded in the protocol still remaining high though shivering had ceased; and on the following morning it was found to be still elevated at +13 though the patient was comfortable, composed and without fever.

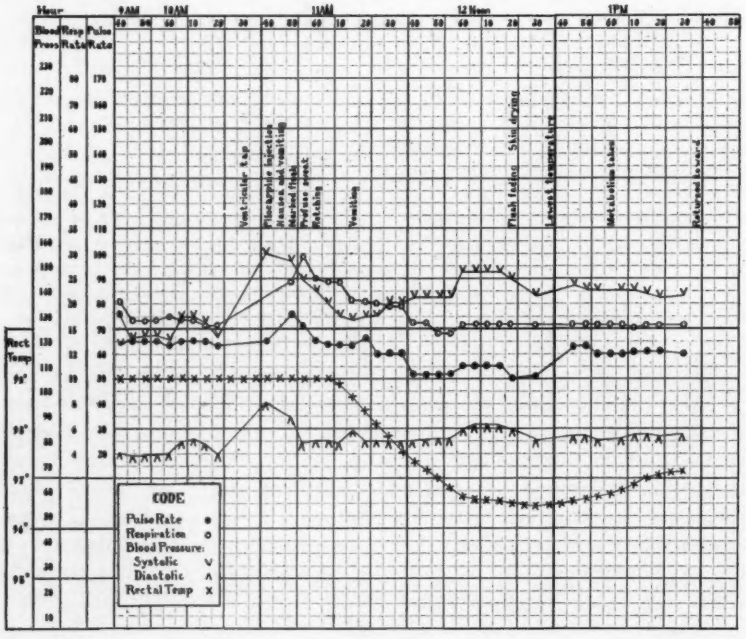

CHART I

Showing the effect on pulse rate, respiration, blood-pressure and rectal temperature of an intraventricular injection of 2.5 milligrams of pilocarpine.

At an earlier session, as mentioned above, a cubic centimeter of pituitrin had given only a mild reaction, and it may be presumed, had we cared to subject this willing man to further tests, that a dose of pilocarpine larger than 2.5 mgm. would have given as striking an antypyretic response as the 1.5 cubic centimeter dose of pituitrin evoked. In the two patients in the series who had received 5-mgm. intraventricular doses of pilocarpine, one showed a fall of 2° in temperature in one and one-half hours and the other a fall of 4.5°. Personal idiosyncrasy doubtless is but one of many factors in the variability of the reactions; the remarkable thing

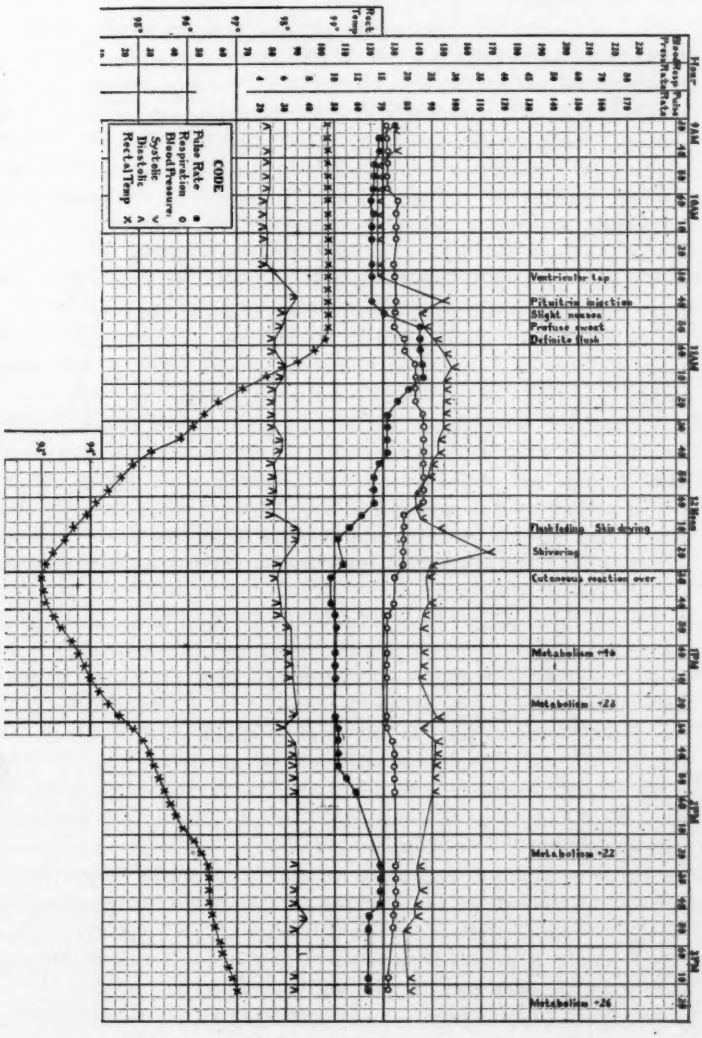

CHART II

Showing (for comparison with Chart I) the effect of 1.5 cubic centimeters of pituitrin injected into the ventricle of the same patient at a subsequent session.

is that the responses to the two substances, under the inexact circumstances of these observations, not only bear such a close resemblance but are chronologically and quantitatively so similar.

Just how and where pilocarpine and its allied drugs act upon the secretory glands seems to be not fully agreed upon by pharmacologists. They are supposed to have an excitatory effect on the peripheral nerve terminations in the various glands and at the myoneural junction of smooth muscle. And since the effect of atropine is antidotal to that of pilocarpine, it has been assumed to have a paralytic effect on the same terminal apparatus whether in salivary, gastric, pancreatic or sudoriferous glands or unstriated muscle. Some authors, indeed, have claimed that the action of muscarine and allied drugs is a direct one on the organs themselves and that the nerves are not in any way involved. However this may be, all authorities agree that the effect of these drugs on the circulation varies in different species, and so far as man is concerned neither has a haemodynamic response been observed nor any effect on the pulse rate in any dose that one would feel justified in administering.

Though the physiological action of pilocarpine is evidently expended somehow in stimulating the autonomic nervous system, the possibility that it might act on a higher center controlling the system rather than on the periphery does not seem to have been given due, if any, consideration. This may, indeed, be true of other drugs, the effects of which are similarly apt to be studied on anaesthetized animals or on pithed animals under artificial respiration.

Though the subject, whose tests have been cited in the protocols above, happened to be convalescent from an operation for a cerebral glioma which had been exposed from the side, the larger number of tests in the series have been made upon patients following frontal osteoplastic operations for pituitary adenomas. In the process of making the customary bone flap for all such procedures four or more preliminary perforations are made through the skull and these small holes make subsequent access to the ventricle by a needle even more simple than the performance of a lumbar puncture. The flap, moreover, is so outlined that its lower leg, for purposes of concealment, passes through the line of the eyebrow which necessitates division of the supraorbital nerves to the corresponding side of the forehead. Hence the scalp overlying the bone flap, though its blood supply is intact, is denervated and remains anaesthetic until, in the course of some months, the nerves reunite.

It has long been known to clinicians that paralysis of the peripheral nerves renders the corresponding skin field irresponsive to the sudorific effects of pilocarpine. This fact, utilized long ago by Victor Horsley to determine the upper level of a spinal cord lesion, has been more recently employed by Otfrid Foerster as a means of mapping out the dermatomes

after the surgical division of the spinal nerve roots. However, owing to overlap of the skin fields supplied by the spinal segments, the boundary of the affected area under these circumstances is less sharply demarcated than in the operations under consideration.

As shown in Miss Codding's color sketch (frontispiece), the perfectly healed flap remains pale and dry in striking contrast to the rest of the face and body which may be greatly flushed and dripping with sweat. With a sufficient dose, either of extract or drug, to give a marked reaction the contrasting color effect in the forehead is brought out by either interventricular pilocarpine or pituitrin and also by an intramuscular injection of pilocarpine. On the other hand, the intramuscular or intravenous injection of pituitrin, as already pointed out, causes a generalized pallor which affects the skin of both sides of the forehead alike. Since the circulation of the bone flap remains intact, this would appear to indicate that the effects both of pituitrin and pilocarpine introduced by way of the ventricle are not exerted on the sweat glands through the medium of the circulating blood or of sympathetic fibres which accompany arterial blood-vessels but must be produced by effector impulses which travel from some higher center by way of the peripheral nerves, presumably along certain sensory fibres, which, in their antidromic function, behave as part of the parasympathetic system.

Both of these substances, moreover, the drug as well as the extract, give reactions that suggest a parasympathetic (bulbar) rather than a sympathetic (thoroco-lumbar) stimulation; and whether it is justifiable to assume that these supposedly reciprocal systems, if they are actually separable, are each under the control of its own higher hypothalamic center further studies may possibly show. Unquestionably the action of other drugs, particularly those of the muscarine series, when introduced into the cerebral cavities is a matter that needs ventilation.

Conclusions.—Pilocarpine and pituitrin have a similar action in producing widespread vaso-dilatation, sweating, vomiting and lowering of the body temperature when injected into the cerebral ventricles. The effects suggest a central autonomic stimulation predominantly of the parasympathetic division.

III. THE ACTION OF ATROPINE IN COUNTERACTING THE EFFECTS OF PITUITRIN AND OF PILOCARPINE INJECTED INTO THE CEREBRAL VENTRICLES

BY HARVEY CUSHHIG

Communicated March 16, 1931

In the two preceding papers it has been shown: (1) that the intraventricular injection of pituitrin leads to a striking response characterized by nausea and vomiting, flushing, sweating, salivation and a marked fall in body temperature usually though not always accompanied by a drop in the basal metabolic rate; and (2) that a reaction of surprisingly similar type promptly follows the intraventricular injection of pilocarpine.

Since we have in atropine an effective antidote to pilocarpine, it was felt that should the reaction of pilocarpine by way of the ventricle be checked by atropine, we might expect the pituitrin reaction to be similarly checked if the two substances, the drug and the extract, in the production of their similar effects, actually operated through the same and probably central nervous mechanism.

On one or two occasions when the reaction to pituitrin had been more marked than expected and the subject was rendered unduly uncomfortable from the recurrent retching and vomiting, it had been observed that an injection of 1 mgm. of atropine and 5 mgm. of morphia effectually checked the reaction. Under this suggestive lead, the matter was first put to test as follows:

A patient, convalescent from a highly successful operation for a chromophobe adenoma, had shown on October 14, 1930, a typical, moderately severe response to the intraventricular injection of 1 c. cm. of pituitrin with sweating, vomiting and a fall of temperature of two degrees in two hours accompanied by a drop in the basal metabolic rate from −11 to −18. On repeating the test four days later, with the coincidental subcutaneous injection of 1 mgm. of atropine, there was no discernible response.

Another patient, likewise convalescent from a similar operation for the same malady, had shown on October 16, 1930, a somewhat tardy (30 minutes) but typical response to 1 c. cm. of pituitrin intraventricularly with moderate sweating, flushing and vomiting over a period of two hours and a drop in temperature of 1.2°F. Eight days later, 5 mgm. of intraventricular pilocarpine provoked a prompt and vigorous reaction with vomiting, sweating, flushing, lachrymation and salivation, and a drop in rectal temperature of 4.4° in 90 minutes, the basal metabolic rate remaining unchanged. After an interval of three days, on October 27, 1930, the intraventricular injection of 1 c. cm. of surgical pituitrin, when repeated with the coincidental subcutaneous injection of 1 mgm. of atropine, caused no appreciable reaction apart from a subjective dryness of the mouth, a possible slight temporary contraction of the pupils, a trifling increase in pulse rate and a moderate pressor response.

It remained to be seen whether atropine would have an inhibitory effect on the response to pituitrin as well as to pilocarpine when coinci-

dentally injected into the ventricle. A favorable opportunity to make the test occurred in the following case:

The patient, a woman 56 years of age, had been operated upon November 10, 1930, for a fairly well encapsulated left parasagittal glioma which was easily removed, apparently intact. From this operation she made an excellent recovery with perfect wound healing and no febrile reaction at any time until the 17th postoperative day when for the first time, following a series of x-ray treatments, she showed a slight wave of pyrexia reaching 102°F.

Having already come to realize the possibility that the temperature-lowering effect of intraventricular pituitrin might be utilized to combat the neurogenic hyperthermias which sometimes occur after serious operations for tumours,* though there was no reason for suspecting that this patient's mild fever was of this type, it at least gave an opportunity of seeing what would be the effect of the injection as an antipyretic.

Accordingly on November 28th at 4.25 P.M., the rectal temperature being 102.4°F., 1 c. cm. of surgical pituitrin was introduced into the ventricle with the usual, though in this instance only a moderately striking reaction, which was somewhat delayed in onset and occurred without appreciable change in pulse rate or blood-pressure. After an interval of 10 minutes there was nausea, lachrymation and salivation; in 15 minutes, the temperature had begun to drop (101.7°); in 35 minutes sweating and flushing were first definitely noted; after 60 minutes there was a copious evacuation of the bowels (temp. 100.8°); in 1 hour 20 minutes there was an initial attack of vomiting followed by other similar attacks during the course of the next two hours by which time the reaction was over, though the rectal temperature continued to fall until 8 P.M. when it was at its lowest point of 98.4°F., a drop of 4 degrees.

Four days later, December 2, 1930, with the rectal temperature at 99.8°, she was given at 9.40 A.M. an intraventricular pilocarpine test (2.5 mgm.) which gave a typical reaction as follows: There was a prompt pressor response from 110/70 to 140/80 which endured throughout the test; at the end of 5 minutes she experienced abdominal uneasiness followed by nausea and retching; after 9 minutes, first appearance of sweating, flushing and salivation soon becoming excessive; 11 minutes, an explosive, copious bowel movement;** 16 minutes, owing to patient's agitation the reaction was checked by a hypodermic injection of morphia 5 mgm. and atropine 0.5 mgm. This injection promptly quieted her and within 5 minutes, though the flush continued, the sweat had ceased together with the salivation, leaving her with a dry mouth. Periodical vomiting nevertheless recurred during the next hour and a half, the last specimen showing a positive guiac test for blood. The rectal temperature slowly dropped in the course of two hours from its initial 99.6° to 97.1°, its lowest level.

This patient, therefore, having shown a moderate reaction to an intraventricular injection of 1 c. cm. of surgical pituitrin and an unduly exaggerated one to the intraventricular injection of 2.5 mgm. of pilocarpine, permitted us to try the effect of the preliminary intraventricular injection of atropine on these responses. Accordingly, on December 4, 1930, 0.5 mgm. of atropine was introduced in the ventricle without any appreciable

* These hyperthermias are more commonly observed in children after the radical removal of median cerebellar tumours which lead to the abrupt collapse of the secondary hydrocephalic distention of the ventricle.

** It will be observed that both intraventricular pituitrin and pilocarpine in this case had an unusually definite effect on the sacral autonomic.

effect other than the sensation of dryness of the mouth and questionable slight increase in the diameter of the pupils. Thirty minutes later, one c. cm. of surgical pituitrin was introduced without any subsequent subjective effect or objective reaction whatever on the part of cardiovascular, gastro-intestinal or thermo-regulatory mechanisms.*

On December 8th at 11.25 A.M., again after the usual preliminaries, another 0.5 mgm. of atropine was injected into the ventricle, the same subjective sensation as before of dryness in the mouth being produced, but there was no determinable pupillary change. Thirty minutes later 2.5 mgm. of pilocarpine was introduced, and though the tongue appeared to become somewhat more moist there was, apart from this, no observable effect of the drug whatsoever.

Whereas, after the typical response to pituitrin or pilocarpine given alone, this patient, as has been true of other subjects similarly tested, showed for some hours inappetence due to subdiaphragmatic uneasiness with waves of nausea, on the conclusion of each of the tests which were counteracted by atropine she eagerly ate a hearty lunch.

Atropine, in the opinion of pharmacologists, exercises a paralytic effect, like curare, at the peripheral nerve termination of the glands as well as at the myoneural junction of involuntary muscle. In other words, the drug supposedly acts at the same peripheral points at which pilocarpine causes its excitatory effects, the two drugs being peculiarly antidotal. These observations herein reported if correctly interpreted would seem to suggest that both drugs may act centrally as well, and if this is so they must probably operate through some diencephalic center where parasympathetic impulses may be discharged or inhibited.

Conclusion.—Atropine whether given subcutaneously or previously introduced in the cerebral ventricles appears completely to counteract the customary effect both of pilocarpine and of pituitrin when administered by way of the ventricles.**

* Whether the atropine served to check the usual oliguric effect of the extract unfortunately could not be determined.

** In the succeeding papers an explanation of certain negative responses to the intraventricular injection of pituitrin and pilocarpine will be offered, and the possible method of action of these substances so introduced will be more fully discussed.

ACTIVATION BY CHARCOAL[1]

BY WILDER D. BANCROFT AND S. F. WHEARTY, JR.

BAKER CHEMICAL LABORATORY, CORNELL UNIVERSITY

Communicated February 19, 1930

In the dark, benzene[2] does not react with chlorine at any temperature up to the boiling-point of the solution under atmospheric pressure.[3] It is usually stated that chlorine reacts with boiling benzene in the dark; but the experiments of Slator[4] and of Goldberg[5] prove that this is really a photochemical reaction and that it does not take place if no light reaches the boiling benzene. In bright sunlight, benzene hexachloride ($C_6H_6Cl_6$) is formed when benzene and chlorine are brought together even at 0°. With rising temperature, the reaction takes place more readily until, at the boiling-point, it occurs unless light is rigidly excluded. Chlorine reacts with benzene in presence of phosphorus pentachloride,[3] producing the hexachloride. In this reaction the phosphorus pentachloride plays the part of a carrier. When chlorine is passed into a solution of iodine monochloride in benzene in the dark, some benzene hexachloride[4] is formed, though substitution products are formed chiefly. In presence of ferric chloride, stannic chloride, aluminum chloride, antimony pentachloride, or molybdenum pentachloride, chlorine and benzene react, forming products only.

With toluene we have the contrast between substitution in the benzene ring and substitution in the methyl group or side chain instead of the contrast between the substitution products and the addition products in the case of benzene. Substitution in the side chain takes place when chlorine and toluene are exposed to sunlight[6] at 0° and when chlorine is led into boiling toluene.[7] It is probable that the latter method of preparation is a photochemical one; but there seems to be no direct evidence on the point. Phosphorus pentachloride acts as a chlorine carrier with toluene, forming benzyl chloride.[8] Such carriers as ferric chloride, stannic chloride, molybdenum chloride and iodine monochloride cause ring substitution exclusively under ordinary conditions.

It is known that charcoal activates chlorine and it is used commercially as a catalytic agent in the formation of phosgene. It was consequently expected that charcoal would act as a catalyst with benzene and toluene, causing the formation of addition products with benzene and substitution in the side chain with toluene. An activated charcoal ("Nuchar" No. 000, from the Industrial Sales Corporation) was used and ring-substituted products were formed exclusively. Since that might be due to the presence of small traces of iron, the charcoal was heated almost to the softening point of hard-glass combustion tubing and chlorine was passed over it

for about four hours so as to drive off the iron as ferric chloride. This did not change things at all; but it is very difficult to prove a negative and people can always claim that the effect was due to minute traces of some metallic chloride and not to the charcoal.

It was, therefore, deemed wiser to assume temporarily that the effect was due to charcoal and to see whether this viewpoint would lead to conclusions which could be tested independently—as proved to be the case. To account for the apparent results, it seems necessary to assume that charcoal activates benzene and toluene and that the activated hydrocarbons react with chlorine to give ring-substituted compounds. If this is true, it should be possible to activate benzene and toluene by light of suitable wave-length and cause ring substitution with chlorine.

It is known that no ring substitution occurs in ordinary sunlight when the reaction takes place in a glass container. The most effective light is that which is absorbed by the chlorine, activating it. Custis[9] has reported that ring substitution does take place with benzene and with toluene when the reaction is carried out in a quartz flask placed a few centimeters from an iron arc. Light from a carbon arc did not cause ring substitution. This seems to prove that light of very short wave-length, such as is found in the spectrum of an iron arc, activates the benzene and toluene, which absorb only in the ultra-violet, causing them to react with chlorine to form ring substitution products. This is similar to what happened when supposedly pure charcoal was used as catalyst, except that benzene hexachloride was also formed in the experiment with the iron arc. We have confirmed the results of Custis. About 300 cc. of dry, thiophene-free benzene was placed in a quartz flask fitted with a reflux condenser and kept saturated with chlorine. The quartz flask was moved to within a few centimeters of an iron arc formed between two iron rods carrying eighteen amperes. After about three hours, or when the delivery tube clogged, the reaction was stopped and the flask allowed to cool. The benzene hexachloride was filtered off and the filtrate distilled to get rid of the excess benzene. The ring-substituted products could be recognized by their unmistakable odor. Hexachlorobenzene was formed in the vapor and caught in the condenser tube. This was identified by its melting-point.

Dry redistilled toluene was treated in a manner similar to that used for benzene. The chlorotoluenes were partially separated from the excess toluene and the benzyl chloride by fractional distillation under reduced pressure. After converting the mixture to the corresponding acids by oxidation with potassium permanganate, and separating the acids by fractional crystallization from ligroin,[10] the presence of chlorotoluene was confirmed by the melting-point of the product.

The general conclusions of this paper are as follows:

1. Purified, activated charcoal causes chlorine to substitute in the ring with benzene and toluene.

2. We have confirmed Custis' results that light from an iron arc causes some ring substitution of chlorine with benzene and with toluene.

3. Certain unspecified wave-lengths in the ultra-violet activate benzene and toluene and give rise to the ring substitution.

4. If the action of the charcoal is not due to metallic impurities, charcoal must be an activating catalyst for benzene and toluene.

[1] This work is part of the programme now being carried out at Cornell University under a grant from the Heckscher Foundation for the Advancement of Research established by August Heckscher at Cornell University.

[2] Bancroft, *J. Phys. Chem.*, **12**, 417 (1908).

[3] Willgerodt, *J. prakt. Chem.*, [2] **34**, 264 (1886).

[4] Slator, *Z. physik. Chem.*, **45**, 513 (1903).

[5] Goldberg, *Z. wiss. Photographie*, **4**, 61 (1906).

[6] Schramm, *Ber.*, **18**, 606 (1885).

[7] Cannizzaro, *Compt. rend.*, **41**, 517 (1855).

[8] Colson and Gautier, *Ann. chim. phys.*, [6] **11**, 19 (1887).

[9] Custis, *J. Franklin Inst.*, **184**, 875 (1917).

[10] Bornwater and Holleman, *Rec. trav. chim.*, **32**, 231 (1913).

AROMATIC SUBSTITUTION PRODUCTS WITH FLUORINE[1]

BY WILDER D. BANCROFT AND S. F. WHEARTY, JR.

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Communicated February 24, 1931

When fluorine is passed into dry benzene at room temperature, small explosions occur and carbon is precipitated, hydrogen fluoride and carbon tetrafluoride passing off. If the fluorine is diluted to one-half with dry nitrogen, and the benzene is cooled to 7°, the reaction takes place more slowly and a tarry product is obtained with an odor somewhat like diphenyl. This was filtered off and the filtrate was shaken with dilute alkali until free from hydrofluoric acid. An attempt was made to establish the presence of fluorobenzene by nitration with 1:1 nitric-sulphuric acid mixture, which converts the benzene into the dinitro derivative, m. p. 90°, b. p. 297°, and fluorobenzene into a 9:1 mixture of para and ortho nitrofluorobenzene, m. p. of the mixture,[2] 18.55°. Sodium methylate converts the latter compound quantitatively into the corresponding anisol, m. p. 54°, with a separation[3] of sodium fluoride. No fluorobenzene could be detected by this method.

The solid material remaining was washed as well as possible with dilute alkali and then tested qualitatively for fluorine by a potassium fusion

and precipitation of calcium fluoride from faintly alkaline solution by calcium nitrate. Fluorine was found to be present by this method. No further analysis was attempted. From the tarry nature of the material and the similarity of its odor to diphenyl, the product was assumed to be a fluorine-substituted condensation product. No test was made for an addition product. Toluene behaved similarly to benzene when diluted fluorine was bubbled through it. No fluorine-substituted toluene could be detected and a tarry residue was formed which gave a qualitative test for fluorine as in the case of benzene.

It was thought that better results might be obtained if experiments were made with a substance containing little or no hydrogen. Hexachlorobenzene and 1–3–5 trichlorobenzene were tried for this purpose. We are indebted for these products to Dr. W. J. Marsh of the Hooker Electrochemical Company.

When fluorine is passed slowly over hexachlorobenzene, a reaction occurs as is shown by the heating of the reaction vessel and by an evolution of chlorine. If the rate of flow is increased, small explosions occur and carbon is formed. If the reaction chamber is cooled, there seems to be little or no reaction. It is, therefore, necessary to regulate carefully the flow of the fluorine, reducing the rate when small explosions begin but not letting it get so low that practically no reaction takes place. In time a colorless, sticky, liquid of peculiar odor starts to form. This drips off the crystals and can be withdrawn for purification and analysis. This material is refluxed until there is no longer any test with starch-iodide or blue litmus paper. When the liquid is subjected to fractional distillation, the fractionation is not sharp; but most of the material comes over within two ranges, 140–150° and 230–240°.

A concentrated solution of fifty grams of 1–3–5-trichlorobenzene in carbon tetrachloride was made up and fluorine was bubbled through this, slowly at first and then rapidly for about fifty-three hours. The mixture was refluxed to get rid of the dissolved gases and then subjected to fractional distillation under diminished pressure. At 2.5 cm. mercury and 75° a pale yellow liquid came over, which boiled at about 150° under atmospheric pressure but was not stable under those conditions.

Chlorine and fluorine were determined simultaneously by a modification of the Drogin and Rosanoff method,[4] using forty grams of potassium and one hundred and thirty grams of alcohol per gram of liquid to be analyzed. When this method was tested on fluorobenzene, it gave too low results; but it was hoped that the complex compounds, which we had, would break down more easily.

The results obtained from the analyses of the compounds produced by fluorination of hexachlorobenzene and 1–3–4-trichlorobenzene are as follows:

A. From Hexachlorobenzene

I. Fraction boiling at 230–240°

% Cl	% F
53.7	16.4
53.7	14.7
Calculated for $C_6Cl_4F_2$	
56.3	15.1

II. Fraction boiling at 140–150°

46.4	20.9
45.3	20.6
Calculated for $C_6Cl_3F_3$	
45.2	24.2

B. From 1–3–5-Trichlorobenzene

I. Fraction boiling at 75° (2.5 cm. Hg)

35.5	28.5
35.1	28.7
Calculated for $C_6HCl_2F_3$	
35.3	28.3

While the agreement between the observed and the calculated values is not strikingly good in the case of the reaction products from hexachlorobenzene, there can be no doubt as to the identity of the compounds. Kraay[5] and DeGrauw[6] have recently prepared 3–4-dichlorofluorobenzene, b. p. 171°, 2–5-dichlorofluorobenzene, b. p. 168°, and 2–4–5-trichlorofluorobenzene, m. p. 62° by the diazo reaction.

The result with the 1–3–5-trichlorobenzene was quite unexpected. It was assumed that the fluorine would react either with the hydrogen alone or with the chlorine alone; but apparently one chlorine atom is substituted and two hydrogen atoms. This must be due to the grouping of the substitution products. More light will be thrown on this if we can produce a similar reaction by means of chlorine and symmetrical tribromobenzene.

The general results of this paper are:

1. By the action of gaseous fluorine on hexachlorobenzene there have been prepared tetrachlorodifluorobenzene and trichlorotrifluorobenzene.

2. By the action of gaseous fluorine on symmetrical trichlorobenzene there have been prepared dichlorotrifluorobenzene.

3. The preparation of dichlorotrifluorobenzene from symmetrical trichlorobenzene means the replacement of one chlorine atom and two hydrogen atoms by fluorine. It is not yet known why the fluorine should not replace hydrogen or chlorine exclusively before starting to replace the other.

[1] This work is part of the programme now being carried out at Cornell University under a grant from the Heckscher Foundation for the Advancement of Research established by August Heckscher at Cornell University.

[2] Holleman, *Rec. trav. chim.*, **24**, 140 (1905).

[3] Holleman, *Ibid.*, **23**, 225 (1904).

[4] Drogin and Rosanoff, *J. Am. Chem. Soc.*, **38**, 711 (1916).

[5] Kraay, *Rec. trav. chim.*, **48**, 1055 (1929).

[6] De Grauw, *Ibid.*, **48**, 1061 (1929).

REVERSIBLE COAGULATION IN LIVING TISSUE. II[1]

BY WILDER D. BANCROFT AND J. E. RUTZLER, JR.[2]

BAKER CHEMICAL LABORATORY, CORNELL UNIVERSITY

Communicated March 3, 1931

Since relief from the addiction to drugs is one of the important problems of the civilized world, it seems wise to see what the outcome is from the application of Claude Bernard's theory of anesthesia to morphinism. Gwathmey[3] says: "*The ganglion cell, according to Binz, is the point of attack of the anesthetic agent.* In his experiments, fresh sections of the brain cortex of rabbits were placed in a one per cent solution of morphine hydrochloride, or exposed to chlorine vapors. The effect of coagulation-necrosis was produced, as is seen when protoplasmic poisons of neutral reaction are allowed to act upon large transparent infusoria. The protoplasm is first darkened, and the movements become sluggish; later the protoplasm becomes granulated, and the movements cease. Recuperation may take place from the first stage by washing away the poisons [it can be seen that this is the same as the peptization of gels by washing out the coagulating agent]; but not from the last stage. The first stage is likened by Binz to the sleep of the cell; the last to death. The first trace of coagulation may redissolve but coagulation itself does not." There is then little doubt but that, in cases of morphinism, we are dealing with an abnormal condition of the brain colloids, or of certain of them; they are coagulated.

In a previous paper Bancroft and Rutzler[4] reported on the experimental application of the Claude Bernard theory of anesthesia; it was shown that sodium thiocyanate can relieve ether, amytal, and morphine anesthesia by peptizing the reversibly coagulated protein colloids of the central nervous system. Sodium thiocyanate was chosen because it peptizes proteins stron 'y and stands at the head of the lyotropic series of anions in this respect. The lyotropic series for egg albumin appears to be as follows: $CNS > I > Br > ClO_3 > NO_3 > Cl > CH_3COO > SO_4 >$ tar-

trate > citrate; the thiocyanate ion peptizes the most and the citrate ion the least in this case.

Having demonstrated that sodium thiocyanate antagonizes morphine, relieving somewhat the state of unconsciousness, a more striking experiment was performed. A rabbit weighing about 2300 grams was injected intravenously with five cc. of a 20% solution of sodium thiocyanate. Fifteen minutes later 0.10 gram of morphine hydrochloride was injected subcutaneously. The rabbit rapidly lost strength probably because of the morphine being forced to other substrates than the brain to some extent. The animal appeared to be completely conscious, and the rate of respiration was 80 per minute 44 minutes after the morphine was injected. The rabbit was still conscious after one hour 42 minutes; there was no decided decrease in the rate of respiration. The dose of sodium thiocyanate was too heroic, for the rabbit died, probably from sodium poisoning; the colloid chemistry of this situation is not germane to the present discussion. The experiment shows that the thiocyanate maintained consciousness in the rabbit despite the presence of the morphine. Furthermore the effect upon the colloids of the respiratory center is most striking when one considers that normally without the presence of the sodium thiocyanate, the rate of respiration would have been somewhere between 10 and 25 per minute. The antagonism of sodium thiocyanate to morphine is very distinct in this case.

By using sodium tartrate which is at the other end of the lyotropic series from sodium thiocyanate, the narcosis produced by morphine should be somewhat deepened, for the tartrate ion will exert little or no peptizing effect, and the positive sodium ion should aid in decreasing the degree of dispersion of the negatively charged brain and sensory nerve colloids. A 10% solution of sodium tartrate was injected intravenously into a rabbit weighing about 2400 grams, five cc. being used. Shortly thereafter 0.1 gram of morphine hydrochloride in water solution was introduced subcutaneously. The respiration rate was only 10 per minute five hours later; the rabbit had not recovered at all completely after six hours 33 minutes.

Ten days later, the same rabbit was again given subcutaneously 0.1 gram of morphine hydrochloride in water solution. This time the minimum rate of respiration was 18 per minute; after five hours the rabbit was completely conscious and crawled around of its own accord and with no difficulty. The narcosis produced by the morphine was sensibly less in the absence of the sodium tartrate.

Sodium thiocyanate therefore tends to antagonize morphine, as it should, and sodium tartrate tends to synergize it (the sodium tartrate did not appear to have any narcotic action in the absence of morphine), thus also falling into line. This then indicates something of what can be

expected when sodium thiocyanate is administered carefully to drug addicts.

As a result of the continued use of morphine it would seem that a colloidal change takes place whereby the brain colloids are kept constantly in a degree of dispersion that is less than normal, i.e., somewhat agglomerated. This stage corresponds to the craving stage. Then, upon using morphine to satisfy the desire, these same colloids become even less finely dispersed, and the craving is assuaged. Upon recovery from the effect of any given dose of the drug, the brain colloids of the addict return not to their normal particle size but only to a partially agglomerated condition; then there is again a desire for the drug. The whole system becomes accustomed to this abnormally dispersed condition of the brain colloids; probably only certain of the brain colloids are involved.

The withdrawal symptoms met with upon attempting to cure drug addicts by withholding the morphine are very much like those described by Borg[5] upon prolonged administration of large amounts of sodium thiocyanate for the relief of hypertension: disorientation, hallucinations of sight and hearing, mania, confusion and ideas of persecution, singly or in combination. These symptoms are not due to the same cause because the sodium thiocyanate over-peptizes the brain colloids of the normal person.

Upon withholding the drug from the addict, the peptizing agents normally present in the body tend to return the suspended particles to their original size. This gives rise to a state of irritability, or hyperexcitability like that which is observed upon recovering from the effects of an anesthetic. It is then that the withdrawal symptoms become manifest; there is also a strong desire for the drug. Sodium bromide, which is near the thiocyanate end of the lyotropic series, can relieve certain coagulated conditions of the brain colloids that give rise to somewhat the same type of symptoms. So, with a slightly agglomerated condition, or with a slightly over-peptized state, much the same mental symptoms are encountered. Therefore, the withdrawal symptoms that are met with seem to fall into line with the colloidal theory of drug addiction.

The employment of peptization therapy, using sodium thiocyanate, should tend to increase the degree of dispersion of the partially agglomerated protein nerve colloids of the brain that are involved in drug addiction. This should increase the tolerance of the individual to morphine; the next stage would then be a return to the truly normal particle size of the suspended proteins of the brain of the particular individual. The patient would then be normal; if the body furnished its own natural peptizing agents in its usual way, and if the patient, having been returned to normal, refrained from using morphine, a cure should result. A case is known in which tolerance to morphine was established in an addict by the ad-

ministration of sodium thiocyanate. Since bromides and iodides tend to go selectively to disturbed areas,[6] sodium thiocyanate should behave in the same way, only the peptizing action would be greater. The thiocyanate ion, according to this theory, is adsorbed among others upon the nerve colloids that are coagulated by morphine. The effect produced is peptization. It follows naturally that the more the colloids adsorb the thiocyanate ion, within limits, the more stable they will be toward a coagulating agent such as morphine. They will also tend to exist as smaller aggregates in the due course of time. Thus, tolerance is the natural consequence of the administration of sodium thiocyanate to drug addicts.

Iodides and bromides, situated as they are next to thiocyanates in the lyotropic series for egg albumin, can be expected to produce, in a qualitative way, the same effect on drug addicts as the thiocyanate ion. MacLeod[7] has treated several patients in which certain of the protein nerve colloids of the brain appear to have been coagulated or, more properly speaking, agglomerated. He first treated a drug addict for stubborn migraine, using sodium bromide in large enough quantities to induce a long sleep. Although the sodium bromide was not administered for the purpose of curing morphinism, upon recovering from its effect to everyone's astonishment the desire for morphine had vanished. During a period of three years following this treatment there was no report of the return of the patient to the use of morphine. Thus, quite by accident a peptizing agent cured a drug addict.

In the second case treated by MacLeod a victim of morphinism and alcoholism was cured of addiction to both simultaneously by the use of great amounts of sodium bromide. The next case was that of a patient who used chloral habitually; the patient was kept asleep for eight days by the use of sodium bromide. At the end of the treatment the sufferer was cured. Chloral, being a well-known anesthetic, acts by agglomerating reversibly the protein colloids of the brain and of the sensory nerves; the action of the sodium bromide in this case was to disperse the agglomerated protein particles in the same way that it acted to cure morphinism. This establishes an experimental parallelism between the action of morphine and chloral, and the action of sodium bromide in antagonizing them both.

MacLeod's next patient was an hysterical neurotic with a bad family history in this respect. The woman became insane following two months of pregnancy. Mania and morphinism were additional factors to be coped with; but the patient was cured by a drastic treatment with sodium bromide. The insanity encountered here must have been the coagulation type to be discussed by Bancroft and Richter in paper number three of this series, for the catatonic state, or peptization insanity, is theoretically incompatible with morphinism as can be readily seen.

The fifth case was one of cocaine and morphine addiction. Here again the peptizing agent, sodium bromide, functioned as the theory predicts that it should; and a cure resulted. With his sixth patient MacLeod was not so fortunate, for the man, a doctor, died of pneumonia during the treatment; that this was the cause of death was ascertained by a post-mortem examination. A case of mania and acute neurasthenia was cured during a treatment with sodium bromide. The author is not absolutely sure that the sodium bromide caused the cure. This was followed by a case of uncontrolled neurasthenic vomiting which was apparently cured by the bromide treatment.

Church[8] in this country studied two cases. In one case of morphinism he succeeded in curing the patient, although respiratory difficulties were encountered. He lost his second case as a result of uraemia which apparently came from nephritis of long standing. This led Church to point out that the treatment involves great danger due to its drastic nature. His opinion is that it is efficacious when and if it can be demonstrated that the patient is not suffering from any organic disturbances other than those being treated.

These men noticed that once in a while bromide urticaria appeared when using this treatment. Sometimes the patients suffered from delusions while being treated, as would be expected. It must be remembered that these doctors did not show that long-continued dosage with small amounts of sodium bromide will not accomplish the same thing as the drastic measures that they employed.

The results obtained by MacLeod and by Church show, quite definitely, that the desire of addicts for morphine is not explainable on any sort of psychological basis; it is a physiologico-colloidal phenomenon. The efficiency of the bromide ion in peptizing the reversibly coagulated nerve colloids is shown strikingly by Church's first case, for, while under the influence of sodium bromide, 60 grains of morphine per day were administered. Despite this the cure was effected.

Since we are postulating that the protein colloids of the central nervous system behave physico-chemically like albumin, it is interesting to note that Taylor[9] says that injections of starch have been found to be beneficial when there are signs of recovery from morphine poisoning. Starch can be used to keep egg albumin from coagulating even in boiling water. This means that the starch is acting as a protective colloid for the albumin. This seems to strengthen further the chain of evidence for the reversible coagulation theory of drug addiction.

Whatever sodium bromide will do by way of curing drug addicts, sodium iodide, due to its strong adsorption by proteins, and its consequent position in the lyotropic series, should also do and with smaller amounts. For the same reason sodium thiocyanate should be more

effective than sodium iodide, and much more so than sodium bromide. Sodium thiocyanate is not a very toxic substance, even though the thiocyanate ion is strongly adsorbed by proteins. Insofar as its toxicity is due to its peptizing action on the nervous systems, it should be much less toxic when fed to a drug addict, because certain of his nerve colloids are partially coagulated by the morphine that is present. Sodium thiocyanate has been found not to impair renal function even when used in comparatively large doses. Many doctors have employed it for the relief of hypertension.

Barring other dangerous organic ailments, there seems to be no theoretical difficulty in the way of the efficient cure of drug addicts by administering increasingly larger doses of sodium thiocyanate, either by mouth or intravenously, and at the same time slowly withdrawing the drug to which the patient is addicted. By such a treatment it might well take a few months to cure the addict. On the other hand, since smaller quantities of sodium thiocyanate than of sodium bromide should accomplish the result, a drastic treatment like that of MacLeod may be found to be distinctly advantageous. Except in cases of hypotension the authors can see no outstanding medical reason, insofar as they are qualified to judge, why such treatments should not be applicable. Difficulties due to hypotension should not be hard to circumvent.

The general results of this paper are:

1. Claude Bernard's theory of anesthesia covers adequately the case of morphinism; a reversible and invisibly minute coagulation takes place.
2. Sodium thiocyanate has been shown experimentally to antagonize morphine in living tissue.
3. Sodium bromide was shown by MacLeod to relieve drug addiction, chloral, and cocaine addiction, also alcoholism. It relieves certain nervous disorders.
4. Sodium thiocyanate increases tolerance to morphine, as it should.
5. Sodium tartrate appears to synergize morphine.
6. With the coagulation theory of morphine action and drug addiction substantiated, there appears to be no reason why certain morphine addicts should not be cured efficiently and completely by the use of sodium thiocyanate.
7. Peptization therapy is certainly indicated in the treatment of drug addiction.

[1] This work is part of the programme now being carried out at Cornell University under a grant from the Heckscher Foundation for the Advancement of Research, established by August Heckscher at Cornell University.

[2] Eli Lilly Research Fellow.

[3] Gwathmey, "Anesthesia," 34 (1914).

[4] Bancroft and Rutzler, *Proc. Nat. Acad. Sci.*, **17**, 105 (1931).

[5] Borg, *Minnesota Med.*, **13**, 293 (1930).

[6] von den Velden, *Chem. Abs.*, **7**, 139 (1913); Osborne, *J. Med. Assoc.*, **79**, 615 (1922); Schiff, *Z. ges. expt. Med.*, **28**, 127 (1922).

[7] MacLeod, *British Med. J.*, **1897**, 76; **1899**, April 15; **1900**, January 20.

[8] Church, *N. Y. Med. J.*, **71**, 904 (1900).

[9] Taylor, *A Treatise on Poisons*, 538, 1875.

MOVEMENT OF THE SO-CALLED HAIRS IN THE AMPULLAR ORGANS OF FISH EARS

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The possibility of movement of the sensory cells in the ampulla of the ear and the effects of such movement upon muscular tonus were considered by Ewald (1892). He assumed that there might be ciliary activity of the sensory cells, the hair cells of the crista, although the movements might be so slight as to be imperceptible. The assumptions of Ewald were apparently based upon theoretical considerations only and not upon specific observations.

Ecker (1844), however, recorded the movement of the hair cells in the ear of Petromyzon marinus. The hair cells which he observed were from the semicircular canal and, according to his report, each cell bore a single ciliary hair which was very long in comparison with the length of the cell. Movement of a hair was described as a bending of the tip followed by a lashing in which the basal portion of the cell took little part. No report of the movement of hair cells in ears, except that given by Ecker, is known to me.

While engaged in the study of the fish ear I have found that movement of the hairs is not limited to cyclostomes but is also present in the teleosts, for instance, in *Ameiurus nebulosus*. In this preliminary paper I shall report only observations relative to such movement and leave other findings for more detailed consideration. My studies have been under the direction of Prof. G. H. Parker, to whom I am indebted for kindly criticism and many valuable suggestions.

In the course of my investigations I have had occasion to use many preparations of living cristae acusticae of Ameiurus. These cristae have been so arranged that the full length of the sensory epithelium of each crista might be viewed with the lower power of the microscope or selected portions under a higher magnification. In sixteen of the preparations, which I have made from as many different individuals, I have seen active

movement of the processes which were parts of the cells of the epithelial coverings of the cristae.

The processes which I have seen moving were those of the so-called hair cells and were either the sensory hairs of the epithelium or were cilia which have not as yet been distinguished from these hairs. Although I have seen variations in the sizes of the hairs and differences in the angles at which they extended from the basal layer, I have no evidence sufficient to indicate that there are two distinct types of hairs, one remaining motionless, the other showing movement. While there is this possibility, as far as I have been able to determine from position, size and structure, the hairs which I have seen moving were the true sensory hairs.

In many cristae no motion whatever was observed. When there was movement the number of the hairs beating in any one crista varied from a single one to many. In several cases where movement was seen only two or three hairs were involved. In other preparations a larger number were concerned and in one crista all hairs present in an area covering perhaps one-fourth of the entire sensory region were actively beating.

Movement in the different preparations was not always the same. Some of the hairs actively lashed back and forth with whip-like strokes, beating as if the proximal half was somewhat stiff and the tip more flexible. Hairs which moved in this fashion were beating in a way which was in accordance with the description of similar phenomena given by Ecker, in which the bending was said to be largely at the tip with the basal portion playing little part. But there was not always this agreement. The lashings of one hair which were very rapid when first seen became slower and, after the crista had been for more than an hour in Ringer's solution, the movements of the hair could be clearly followed. In this hair a wave which started at the base moved outward toward the tip, followed immediately by another so that at any given time two complete waves or one wave and parts of two others could be seen in the same hair. This type of movement was distinctly different from the whip-like lashing first mentioned. Other hairs were seen to retain their usual straightness while in motion, showing no curves or wave-like movements but moving back and forth without marked change of form.

The beating of many hairs in a way which might be considered coordinated was observed in one preparation. The movements in this case involved hairs along the proximal portion of the crista over a distance of approximately one hundred micra. The hairs, apparently beating in unison, were under observation for more than an hour during which time no change in the rate of movement was noted.

There were, as far as I have been able to detect, no definite periods of movement and of rest. Individual hair cells have been under observation for one and one-half hours during which time movement continued.

Others which had not been beating when a preparation was first examined have been seen to begin moving, lash back and forth a few times, and then remain still. One hair began to move actively and continued its movements for three minutes, after which time it remained entirely motionless. Another, which upon first examination was found to be actively moving, was observed for fifteen minutes from the time when it was first noted and, throughout this period, there was no noticeable change in the rate or type of movement. These observations indicate no definite length of time during which movement may continue.

The rate of movement, as far as has been determined from these preparations, was not constant. In some instances movement was comparatively slow with perhaps one beat per second; in others it was much more rapid. Counts were made of the number of beats for one of the more rapidly moving hairs and the average of these was found to be approximately three hundred per minute. While the figure is possibly not exact it is significant in that it indicates the rapidity of the movements which were seen in some of the cristae.

Since it has not been possible for me to examine the ear of Petromyzon marinus, the species used by Ecker, I can make no statement as to movement of the hairs in that particular form, but my observations do confirm the fact of movement of the so-called hairs in the inner ear.

Summary.—1. Sensory hairs of the ampullar organs of Ameiurus nebulosus in some cases move actively.

2. Some cristae were seen in which no movement was observed.

3. When movement was seen the number of hairs moving in any one crista varied from one to many.

4. Present evidence does not indicate that there is more than one type of hair cell.

5. In some cases the movement of the hairs was a lashing with whip-like strokes; in others the hairs moved without curving; in still others there was wave-like movement involving the entire length of the hair.

6. Some hairs were seen beating in unison.

7. There were no definite periods of movement and of rest.

8. The rate of movement of the hair cells was not the same for all of the hairs which were seen moving.

Ecker, A., "Flimmerbewegung im Gehörorgan von Petromyzon marinus," *Arch. Anat. Physiol. und wiss. Med.*, Jahrg. 1844, 520–521.

Ewald, J. R., *Physiologische Untersuchungen über das Endorgan des Nervus octavus*, Wiesbaden, 325 pp., 1892.

FURTHER OBSERVATIONS ON THE NATURE OF THE X-PRIME (X′) CHROMOSOME IN SCIARA[1]

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In *Sciara coprophila* Lintner, one of the species of *Sciara* which gives unisexual progenies, it has already been observed[2] that the sex chromosomes of female-producing females are not both identical with those of male-producing females. One of them (X) is identical with those of the male-producer, but the other (X′) differs at least to the extent of possessing something which makes the female a female-producer. The scheme used to represent these chromosomes is indicated below:

Male-producing female XX.
Female-producing female X′X.

The evidence just referred to has also shown that the X-chromosome is freely transmitted back and forth between males and both types of females, whereas the X′-chromosome, or the part of it under consideration, is ordinarily restricted to female-producing females.

In our attempt to ascertain the nature of the sex-determining mechanism here, a special effort is being made to determine the extent and nature of the difference between X′ and X. It has already been shown (loc. cit.) that these two chromosomes[3] are similar in their influence on the general morphology of the fly and that X′ possesses the normal allelomorphs of the two known sex-linked (recessive) genes thus far found in the X. From this it is concluded that X′ and X are fundamentally similar in make up—i.e., that the difference is not of the same order as that distinguishing the X- and Y-chromosomes of many organisms.

On the other hand it has been impossible, thus far, to get either of the two known recessive genes transferred from the X to the X′-chromosome (i.e., combined with the X′ differential) and, as shown in the present paper, it has likewise been impossible to get the gene dealt with here transferred from the X′ to the X-chromosome (i.e., separated from the X′ differential).

The present case involves the recently obtained, dominant, sex-linked, mutant wing character "wavy," the gene for which is carried by the X′-chromosome. Experiments with this character have served both to verify our previous interpretation of the inheritance of the X′ chromosome, and to provide further evidence of a lack of interchange between X′ and X.

The character "wavy" was found by one of us (Smith) in one female from an x-rayed mother. It seems probable that the mutation was

caused by the x-ray treatment, although this is by no means certain. Tests have shown the character to be dominant and to be constant—i.e., practically always manifest somatically when the gene is present. The viability of wavy flies is lower than that of the wild-type; consequently the wavy class is uniformly deficient when compared with the wild-type—averaging about 25% below the latter. (Thirty-eight pair matings of heterozygous wavy females by wild-type males gave 1663 wild-type and 1252 wavy daughters.)

Tests of Wavy and Wild-Type Sisters.—The linkage between wavy and the X′ differential was made evident early in the experiments by the fact that wavy females were consistently female-producers and their sisters were always male-producers. Wavy was crossed only with wild-type in these experiments. Tests were made of 321 wavy females and 25 of their wild-type sisters without an exception to this mode of inheritance. These observations led to tests with the recessive character "swollen" considered below.

Tests of Wavy with the Sex-Linked Recessive Character Swollen.—The gene for swollen is carried by the X-chromosome and hence is transmitted to both males and females. Its inheritance has been described in earlier papers[4] and in greater detail in a paper now in press (*Genetics*). The viability of swollen females is even lower than that of wavy females, as shown by the data of the present paper. In previous experiments, as well as those considered here, swollen females have regularly been male-producers and their non-swollen sisters female-producers.

When wavy virgin females are mated to swollen males the offspring are, as expected, wild-type and wavy daughters in a 1:1 ratio (making allowance for the difference in viability).[5] The wavy daughters here are heterozygous for wavy (in the X′ chromosome) and swollen (in the X). By mating these females singly to swollen males, tests of linkage between wavy and swollen have been made. The following counts are partly from such matings and partly from similar ones in which the mothers came from matings of this type.

Heterozygous Females by Swollen Males.—Experiment H-1507. Four pair matings gave a total as follows (all females): 132 wavy; 58 swollen; 42 swollen (wavy?); 1 wild-type? (proved to be wavy).

In this first experiment some difficulty was experienced in classifying extreme swollen flies as to the presence or absence of wavy, because swollen also affects the wings. For this reason numerous swollen flies were recorded as possibly wavy (see subsequent paragraph for tests of these). Also, as indicated, one fly was classified as possibly wild-type, but on being tested proved to be wavy. In subsequent experiments it was possible to make the initial classification more accurately, but even here a few swollen flies were recorded as possibly wavy (considered below).

Experiment H-1517. Three pair matings gave the following:
Females: 51 wavy; 36 swollen; no wavy swollen; no wild-type.
Males: 1 swollen.

Experiment H-1800. Eleven pair matings gave the following:[6]
Females: 382 wavy; 325 swollen; no wavy swollen; no wild-type.
Males: 3 swollen.

In addition to the above, several experiments may be noted which involved only from one to three matings each. These include fourteen pair matings which gave the following totals:

Females: 491 wavy; 301 swollen; 7 swollen (wavy?); 2 wild-type?
Males: 3 swollen.

Results from Stock Cultures.—Although the above experiments include 2174 individuals, even more convincing evidence is that obtained from stock cultures in which no actual counts are made but in which many flies are tested in the regular routine of keeping the stocks. Here, as in the case of swollen and narrow (in the X-chromosome) considered previously, no crossing-over has been detected between the gene under consideration and the X′ differential.

Tests of Questionable Flies.—The above evidence, as it stands, indicates strongly that no cross-overs occurred here between wavy and swollen, since the wild-type class is absent, save for three questionable individuals, and the wavy swollen class is represented in the later experiments by only a few questionable flies. However, fourteen of the questionable flies were tested as a check on the classification. Two of those in the former class (wild-type?) gave no offspring; the third proved to be wavy, not wild-type. The eleven from the group classified as possibly wavy swollen were mated to wild-type males. All proved to be male-producers, giving swollen sons and a few "exceptional" wild-type daughters, showing that they were typical swollen females, not wavy. The total count from these was 545 swollen males and 18 "exceptional" females.

Absence of Wavy "Exceptional" Males.—It will be observed that in the above records from crosses of heterozygous females by swollen males, a few "exceptional" swollen males appear, but no wavy males. This seems to be characteristic of such matings as indicated by results from stock cultures, and leads to the inference that wavy is lethal when homozygous. Since no wavy males have been secured it has been impossible, of course, to get homozygous wavy females and make further tests.

Discussion.—In the present paper the "X′ differential" has been treated as if it were a single gene or a definitely localized group of genes behaving as a unit. If it is such a unit it should show recombination or crossing-over with other loci in the same chromosome or with those in its homologue

the X-chromosome, unless no crossing-over occurs between these chromosomes. In earlier papers (loc. cit.) results were reported from tests with two recessive mutant genes in the X-chromosome, and in the present paper results are similarly given from tests with a gene in the X′-chromosome. On the present view, these three genes, together with the X′ differential include four loci. It seems improbable that four loci thus detected would chance to lie so close together as to show complete linkage if cross-overs occurred frequently between these two chromosomes. We conclude tentatively, therefore, that crossing-over between X′ and X occurs at a low rate, if at all.

This would indicate either that the cross-over rate is low in *Sciara* generally, at least as regards the sex chromosomes, or that crossing-over between X′ and X is less frequent than between X and X. Present evidence is insufficient to settle the point because only two loci have been detected in the X-chromosome and these give only about 0.5% crossing-over, or less.

[1] This investigation has been aided by a grant from the NATIONAL RESEARCH COUNCIL, Committee for Research on Problems of Sex.

[2] Metz, C. W., *Amer. Nat.*, **63**, 214–228 (1929); Metz and Schmuck, these PROCEEDINGS, **15**, 863–866 (1929); *Ibid.*, **15**, 867–870.

[3] Strictly speaking, of course, the designation X′ applies only to the differential distinguishing the X′ chromosome from the X; but since the extent of this difference is unknown the symbol is used here to indicate the chromosome as a whole. Where the more restricted meaning is intended the term "X′ differential" is used.

[4] Metz and Ullian, '29, these PROCEEDINGS, **15**, 82–85 (1929); Metz and Schmuck, loc. cit., 1929.

[5] Occasional "exceptional" males also occur here as in other unisexual female progenies.

[6] An additional mating in this experiment gave 1 swollen female and 46 swollen males, showing that the mother was pure swollen and did not carry wavy. Since she came from a progeny consisting of wavy and swollen females the error was presumably due to mistaking swollen for wavy.

ON THE UNIFIED FIELD THEORY. V

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The general existence theorem established in Note III ceases to apply when the data of the problem is ascribed over a characteristic surface S_3. In treating this important exceptional case we arrive at an existence theorem which is, roughly speaking, analogous to the existence theorem for the ordinary wave-equation when the data is given over a characteristic surface and which also bears certain resemblances to a theorem of Hadamard.[1] This theorem is capable of dynamical application. It follows from it that there exists an infinite number of sets of integrals h_α^i of the field equations such that each set of integrals and their first derivatives assume the same values over a characteristic surface S_3; in fact, the conditions under which these integrals exist are such as to preclude the occurrence of more than a single set of integrals in case the surface S_3 is not a characteristic. This result leads to the interpretation of the characteristic surfaces as gravitational and electro-magnetic wave surfaces in the four-dimensional continuum. A brief discussion of these wave surfaces will be given in Note VI.

1. Let us denote for the moment by $X^1, \ldots, X^4$ the coördinates of the continuum; let us also denote by H_i^α the contravariant components of the fundamental vectors and by $G^{\alpha\beta}$ the contravariant components of the fundamental metric tensor. A characteristic surface S_3 is then a three-dimensional surface $\Phi(X) = 0$ such that over it the equation

$$G^{\alpha\beta} \frac{\partial \Phi}{\partial X^\alpha} \frac{\partial \Phi}{\partial X^\beta} = 0 \tag{1.1}$$

is satisfied. Suppose that P is not a *singular point* on the hypersurface $\Phi = 0$, i.e., all first derivatives of the function Φ do not vanish at P, and consider another surface S_3^* defined by $\Psi(X) = 0$ which passes through the point P. This latter surface will be subjected to the following condition, the reason for which will later appear.

C_1. *The inequality*

$$G^{\alpha\beta} \frac{\partial \Phi}{\partial X^\alpha} \frac{\partial \Psi}{\partial X^\beta} \gtrless 0 \tag{1.2}$$

holds at the point P.

The above condition is independent of the orientation of the fundamental vectors. It is therefore possible, and we shall later find it expedient, to

orientate the vector configurations throughout the continuum in the following manner.

C_2. *The vector configurations are so oriented that the inequalities*

$$H_2^\alpha \frac{\partial \Phi}{\partial X^\alpha} \gtrless 0 \tag{1.3}$$

$$\sum_{\alpha=1}^{4} \sum_{\beta=1}^{4} \begin{vmatrix} H_1^\alpha & H_1^\beta \\ H_2^\alpha & H_2^\beta \end{vmatrix} \frac{\partial \Phi}{\partial X^\alpha} \frac{\partial \Psi}{\partial X^\beta} \gtrless 0 \tag{1.4}$$

$$\sum_{\alpha=1}^{4} \sum_{\beta=1}^{4} \begin{vmatrix} H_3^\alpha & H_3^\beta \\ H_4^\alpha & H_4^\beta \end{vmatrix} \frac{\partial \Phi}{\partial X^\alpha} \frac{\partial \Psi}{\partial X^\beta} \gtrless 0 \tag{1.5}$$

are satisfied at the point P^2.

We shall refer to the above conditions C_1 and C_2 as *normal conditions*. It is evident that C_2 might also be regarded as giving conditions on the surfaces S_3 and S_3^*. However, the above point of view has been preferred as it does not involve an apparent restriction on the characteristic surface S_3.

In consequence of condition C_1 it follows that the rank of the matrix

$$\left\| \begin{matrix} \frac{\partial \Phi}{\partial X^1} & \frac{\partial \Phi}{\partial X^2} & \frac{\partial \Phi}{\partial X^3} & \frac{\partial \Phi}{\partial X^4} \\ \frac{\partial \Psi}{\partial X^1} & \frac{\partial \Psi}{\partial X^2} & \frac{\partial \Psi}{\partial X^3} & \frac{\partial \Psi}{\partial X^4} \end{matrix} \right\| \tag{1.6}$$

must be two at the point P. In fact, if the rank of this matrix were less than two, condition C_1 would fail to be satisfied. It is therefore possible to choose functions $\Omega(X)$ and $\Xi(X)$ such that the jacobian of the coördinate transformation

$$x^1 = \Phi(X),\ x^2 = \Psi(X),\ x^3 = \Omega(X),\ x^4 = \Xi(X)$$

will not vanish at P; this means that the above transformation possesses an inverse throughout the neighborhood of the point P. Under this transformation the equation of the characteristic surface S_3 assumes the form $x^1 = 0$, while the equation of the auxiliary surface S_3^* becomes $x^2 = 0$. Denoting the components of the fundamental vectors and the fundamental metric tensor in the (x) coördinate system by the usual designation of h and g, respectively, we have from (1.1) that the contravariant component $g^{11} = 0$ over S_3; also by C_1 we have that $g^{12} \gtrless 0$ at P. Moreover, the condition C_2 results in the fact that the inequalities

$$h_2^1 \gtrless 0,\ h_1^1 h_2^2 - h_2^1 h_1^2 \gtrless 0,\ h_3^1 h_4^2 - h_4^1 h_3^2 \gtrless 0 \tag{1.7}$$

are satisfied by the contravariant components h_i^α at the point P. In

treating the problem of the determination of integrals of the field equations by the specification of data over a characteristic surface S_3 we shall assume in the following work the normalization of this problem afforded by the selection of the (x) coördinate system and the assertion of the conditions C_1 and C_2.

2. We shall find it expedient in making certain calculations to introduce a slight change in notation. Let us put

$$\alpha = h_1^1,\ \beta = h_2^1,\ \gamma = h_3^1,\ \delta = h_4^1$$

$$a = h_1^2,\ b = h_2^2,\ c = h_3^2,\ d = h_4^2$$

for the contravariant components h_i^α; also

$$W = \alpha^2 - \beta^2 - \gamma^2 - \delta^2, \quad W^* = \alpha a - \beta b - \gamma c - \delta d.$$

The two-rowed determinants formed from the matrix

$$\left\| \begin{matrix} \alpha & \beta & \gamma & \delta \\ a & b & c & d \end{matrix} \right\|$$

will also enter into our calculations so that we shall use the abbreviations

$$\begin{matrix} A = \alpha b - \beta a, & B = \alpha c - \gamma a, & C = \alpha d - \delta a \\ D = \beta c - \gamma b & E = \beta d - \delta b, & F = \gamma d - \delta c. \end{matrix}$$

The above quantity W is nothing more than the contravariant component g^{11} and hence vanishes over the characteristic surface S_3; also W^* stands for the contravariant component g^{12} so that $W^* \gtrless 0$ at P. Finally the inequalities $\beta \gtrless 0$, $A \gtrless 0$ and $F \gtrless 0$ are equivalent to (1.7).

3. Consider the matrix represented by Table 1. Each row in table 1 corresponds to an equation III (2.2) or III (3.1) determined by the indicated values of j, k, l or j, respectively, and the elements in any column are the coefficients of the derivatives at the top of this column; more precisely each row in Table 1 corresponds to a set of four equations but the above terminology is convenient and has been used throughout this note. It is necessary to deduce a number of lemmas regarding certain matrices and determinants formed from the elements in Table 1.

Let us denote by M_1 the matrix formed from the elements in the first six columns in Table 1. The fourth order determinant in the upper left-hand corner of M_1 will be denoted by J. More generally a determinant constructed from the elements in rows $l, m, \ldots, n$ and columns $p, q, \ldots, r$ in Table 1 will be designated by the symbol

$$\left| \begin{matrix} l & m & \ldots & n \\ p & q & \ldots & r \end{matrix} \right|.$$

Let us consider the eight determinants of order five in M_1 which are formed

by bordering J in all possible manners. Expansions of these determinants show that

$$\begin{vmatrix}1&2&3&4&5\\1&2&3&4&5\end{vmatrix} = \begin{vmatrix}1&2&3&4&6\\1&2&3&4&6\end{vmatrix} = -\alpha\beta\gamma W, \quad \begin{vmatrix}1&2&3&4&5\\1&2&3&4&6\end{vmatrix} = -\begin{vmatrix}1&2&3&4&6\\1&2&3&4&5\end{vmatrix} = \alpha^2\delta W.$$

$$\begin{vmatrix}1&2&3&4&7\\1&2&3&4&5\end{vmatrix} = \begin{vmatrix}1&2&3&4&8\\1&2&3&4&6\end{vmatrix} = -\beta^2\gamma W, \quad \begin{vmatrix}1&2&3&4&7\\1&2&3&4&6\end{vmatrix} = -\begin{vmatrix}1&2&3&4&8\\1&2&3&4&5\end{vmatrix} = \alpha\beta\delta W.$$

Since $W = 0$ at a point P on a characteristic surface S_3 it follows by a theorem in algebra[3] that if $J \neq 0$ at P the rank of the matrix M_1 is four at P. We can, in fact, easily prove a more specific result, namely, that every determinant of order five in M_1 contains W as a factor.[4] As we shall later have use of this result we state it as the following

jkl / j	$\frac{\partial h^j_{2,1}}{\partial x^1}$	$\frac{\partial h^j_{4,3}}{\partial x^1}$	$\frac{\partial h^j_{4,1}}{\partial x^1}$	$\frac{\partial h^j_{3,2}}{\partial x^1}$	$\frac{\partial h^j_{4,2}}{\partial x^1}$	$\frac{\partial h^j_{3,1}}{\partial x^1}$	$\frac{\partial h^j_{4,1}}{\partial x^2}$	$\frac{\partial h^j_{3,2}}{\partial x^2}$	$\frac{\partial h^j_{4,2}}{\partial x^2}$	$\frac{\partial h^j_{3,1}}{\partial x^3}$	$\frac{\partial h^j_{2,1}}{\partial x^3}$	$\frac{\partial h^j_{4,3}}{\partial x^3}$
123	$-\gamma$	0	0	$-\alpha$	0	β	0	$-a$	0	b	$-c$	0
$j=4$	0	$-\gamma$	α	0	$-\beta$	0	a	0	$-b$	0	0	$-c$
$j=3$	0	δ	0	$-\beta$	0	α	0	$-b$	0	a	0	d
124	$-\delta$	0	β	0	$-\alpha$	0	b	0	$-a$	0	$-d$	0
134	0	$-\alpha$	γ	0	0	δ	c	0	0	$-d$	0	$-a$
$j=2$	α	0	0	γ	$-\delta$	0	0	c	d	0	a	0
234	0	$-\beta$	0	$-\delta$	γ	0	0	$-d$	c	0	0	$-b$
$j=1$	β	0	δ	0	0	γ	d	0	0	c	b	0

TABLE 1

LEMMA I. *Every determinant of order five of the matrix M_1 has the form $WR(\alpha, \beta, \gamma, \delta)$, where $R(\alpha, \beta, \gamma, \delta)$ denotes a polygnomial in the variables indicated.*

Let us denote by M_2 the matrix determined by the elements in the first four rows and first six columns in Table 1. The following lemma can then be proved.

LEMMA II. *The matrix M_2 is of rank four at a point P of a characteristic surface.*

This lemma shows in particular that the rank of M_1 is four at P. To prove Lemma II we consider the determinant

$$\begin{vmatrix}1&2&3&4\\3&4&5&6\end{vmatrix} = (\alpha - \beta)^2$$

contained in M_2. The assumption that the above determinant vanishes gives $\alpha^2 = \beta^2$ and since $W = 0$ at P it follows that $\gamma = \delta = 0$ at P. Hence $F = 0$ at P contrary to condition C_2 in Sect. 1. This proves Lemma II.

By calculation we have that[5]

$$\begin{vmatrix} 1 & 2 & 3 & 4 & 5 & 6 & 7 & 8 \\ 3 & 4 & 5 & 6 & 7 & 8 & 9 & 10 \end{vmatrix} = 4A^2F^2 + (B^2 + C^2 - D^2 - E^2)^2.$$

Since $A \gtrless 0$ and $F \gtrless 0$ we obtain the result stated in the following

LEMMA III. *The inequality*

$$\begin{vmatrix} 1 & 2 & 3 & 4 & 5 & 6 & 7 & 8 \\ 3 & 4 & 5 & 6 & 7 & 8 & 9 & 10 \end{vmatrix} > 0$$

is satisfied at the point P.

4. We shall apply the symbols U and V to represent components h^i_{jk} as indicated by the scheme

$$U \sim h^i_{2,1},\ h^i_{4,3};\quad V \sim h^i_{4,1},\ h^i_{3,2},\ h^i_{4,2},\ h^i_{3,1}.$$

Equations III (2.2) and III (3.1) can now be solved for first derivatives of the V with respect to x^1 and x^2 in consequence of the fact that the determinant

$$\begin{vmatrix} 1 & 2 & 3 & 4 & 5 & 6 & 7 & 8 \\ 3 & 4 & 5 & 6 & 7 & 8 & 9 & 10 \end{vmatrix}$$

does not vanish at P by Lemma III. This solution gives

$$\frac{\partial V}{\partial x^1} = \sum R(h)\,\frac{\partial U}{\partial x^\alpha} + \sum R(h)\,\frac{\partial V}{\partial x^\beta} + \bigstar \qquad (4.1)$$

$$(\alpha = 1, 2, 3, 4;\ \beta = 3, 4)$$

$$\frac{\partial V}{\partial x^2} = W \sum R\,\frac{\partial U}{\partial x^1} + \sum R\,\frac{\partial U}{\partial x^\alpha} + \sum R\,\frac{\partial U}{\partial x^\beta} + \bigstar \qquad (4.2)$$

$$(\alpha = 2, 3, 4;\ \beta = 3, 4)$$

where R denotes a rational function of the h^i_α and the $\bigstar$ as usual denotes terms of lower order than those which have been written down explicitly. The occurrence of the quantity W as a factor in the first term of the right member of (4.2) follows as a result of Lemma III; this fact is essential in our later work.

By multiplying the four equations corresponding to the first four rows in Table 1 by suitably chosen quantities p, q, r, s and adding to the equation corresponding to the seventh row in Table 1 it is possible to obtain an equation in which the coefficients of the derivatives of the components U and V with respect to x^1 will vanish at P. This follows from Lemmas

I and II. Similarly it is possible to multiply the four equations corresponding to the first four rows in Table 1 by quantities $\bar{p}, \bar{q}, \bar{r}, \bar{s}$, and add to the equation corresponding to the last row in Table 1 so as to obtain an equation in which the coefficients of the above derivatives will likewise vanish at P. We can, in fact, construct in an obvious manner a system of linear equations in the unknown quantities p, q, r, s or $\bar{p}, \bar{q}, \bar{r}, \bar{s}$ with the non-vanishing determinant

$$\Delta = \begin{vmatrix} 1 & 2 & 3 & 4 \\ 3 & 4 & 5 & 6 \end{vmatrix}$$

and solve by Cramer's rule. This gives

$$p = \frac{-\alpha\delta}{\alpha^2 - \beta^2}, \quad q = \frac{-\beta\gamma}{\alpha^2 - \beta^2}, \quad r = \frac{\beta\delta}{\alpha^2 - \beta^2}, \quad s = \frac{\alpha\gamma}{\alpha^2 - \beta^2},$$

$$\bar{p} = \frac{\beta\gamma}{\alpha^2 - \beta^2}, \quad \bar{q} = \frac{-\alpha\delta}{\alpha^2 - \beta^2}, \quad \bar{r} = \frac{-\alpha\gamma}{\alpha^2 - \beta^2}, \quad \bar{s} = \frac{\beta\delta}{\alpha^2 - \beta^2}.$$

In the two equations so obtained the coefficients of the derivatives in in the last six columns of Table 1, i.e., the derivatives of the quantities U and V with respect to x^2, will be given by the matrix

$$\left\| \begin{matrix} u & v & w & x & y & z \\ -v & u & -x & w & -z & y \end{matrix} \right\|$$

in which $u = \dfrac{\gamma A}{\alpha^2 - \beta^2}, v = \dfrac{\beta E - \alpha C}{\alpha^2 - \beta^2}, w = \dfrac{\alpha B - \beta D}{\alpha^2 - \beta^2},$

$$x = \frac{-\delta A}{\alpha^2 - \beta^2}, y = \frac{-\alpha F}{\alpha^2 - \beta^2}, z = \frac{\gamma D + \delta E - bW}{\alpha^2 - \beta^2}.$$

Let us call the four equations corresponding to the first four rows in Table 1 the system L_1 and the two equations which we have constructed by the above process, the system L_2. Now differentiate L_1 with respect to x^2 and L_2 with respect to x^1. On combining the resulting equations we have a system L_3 of six equations which can be solved for the second derivatives with respect to x^1, x^2 of the quantities U and V. Table 2 indicates the determinant of the coefficients of these derivatives in L_3. Expanding[5] this determinant and neglecting additive terms containing W we obtain the simple quantity $(2\beta W^*)^2$ which does not vanish at P in consequence of the normal conditions imposed in Sect. 1; this fact permits the unique determination of the

0	$-\alpha$	0	β	$-\gamma$	0
α	0	$-\beta$	0	0	$-\gamma$
0	$-\beta$	0	α	0	δ
β	0	$-\alpha$	0	$-\delta$	0
u	v	w	x	y	z
$-v$	u	$-x$	w	$-z$	y

TABLE 2

above second derivatives and leads to a system of equations L_3 of the form

$$\left.\begin{matrix}\dfrac{\partial^2 U}{\partial x^1 \partial x^2} \\ \dfrac{\partial^2 V}{\partial x^1 \partial x^2}\end{matrix}\right\} = W\sum R\frac{\partial^2 U}{\partial x^1 \partial x^1} + \sum R\frac{\partial^2 U}{\partial x^\alpha \partial x^\beta} + \sum R\frac{\partial^2 V}{\partial x^\alpha \partial x^\beta} + \bigstar. \quad (4.3)$$
$$(\alpha \neq 1 \text{ if } \beta = 1, 2)$$

It is to be observed that the first term in the right member of these equations contains W as a factor and that terms involving second derivatives of V with respect to x^1 do not appear.

5. Let us write I (4.5) or III (2.1) in the form

$$\frac{\partial h_2^i}{\partial x^1} = \frac{\partial h_1^i}{\partial x^2} + \sum RU + \sum RV \quad (5.1a)$$

$$\left.\begin{matrix}\dfrac{\partial h_3^i}{\partial x^1} = \dfrac{\partial h_1^i}{\partial x^3} + \sum RU + \sum RV \\ \dfrac{\partial h_3^i}{\partial x^2} = \dfrac{\partial h_2^i}{\partial x^3} + \sum RU + \sum RV\end{matrix}\right\} \quad (5.1b)$$

$$\left.\begin{matrix}\dfrac{\partial h_4^i}{\partial x^1} = \dfrac{\partial h_1^i}{\partial x^4} + \sum RU + \sum RV \\ \dfrac{\partial h_4^i}{\partial x^2} = \dfrac{\partial h_2^i}{\partial x^4} + \sum RU + \sum RV \\ \dfrac{\partial h_4^i}{\partial x^3} = \dfrac{\partial h_3^i}{\partial x^4} + \sum RU + \sum RV\end{matrix}\right\} \quad (5.1c)$$

Other equations of this type likewise result from the condition $W = 0$ over the surface S_3; in fact we have

$$\sum_{\sigma=2}^{4} g^{1\sigma} h_\tau^1 \frac{\partial h_\sigma^\tau}{\partial x^\alpha} = 0 \ (\alpha = 2, 3, 4) \quad (5.2)$$

over S_3. Now $\alpha \neq 0$ at P since $\alpha = 0$ would give $\beta = \gamma = \delta = 0$ at P and we would have a contradiction with the normal conditions imposed in Sect. 1. Making use of this fact and also the fact that $W^* \neq 0$ at P equations (5.2) can be solved for the derivatives of the covariant component h_2^1 with respect to x^2, x^3 and x^4. Hence (5.2) can be given the form

$$\frac{\partial h_2^1}{\partial x^2} = \ldots; \frac{\partial h_2^1}{\partial x^3} = \ldots; \frac{\partial h_2^1}{\partial x^4} = \ldots, \quad (5.3)$$

where the dots denote terms of the sort occurring in the right members of (5.1) with the exception of the derivatives in the left members of (5.3). It is to be borne in mind that equations (5.3) hold only over the surface S_3 and must not, therefore, be differentiated with respect to the coördinate x^1 in the process of finding derivatives of the component h_2^1 which we shall later employ. This circumstance, however, causes no difficulty since such differentiations can be made on the equation (5.1a) which contains the derivative of h_2^1 with respect to x^1 in its left member.

6. Suppose that each component U is defined over the surfaces S_3 and S_3^* as an analytic function of the surface coördinates. We represent this by writing

$$\left.\begin{aligned} U &= J(x^2, x^3, x^4) \quad \text{for } x^1 = 0 \\ U &= K(x^1, x^3, x^4) \quad \text{for } x^2 = 0 \end{aligned}\right\} \tag{6.1}$$

where it is to be understood that over the two-dimensional surface S defined by $x^1 = x^2 = 0$ the functions J and K are identical, i.e.,

$$J(0, x^3, x^4) = K(0, x^3, x^4).$$

Over the surface S_2 we shall ascribe the components V as indicated by the equation

$$V = L(x^3, x^4) \quad \text{for } x^1 = x^2 = 0. \tag{6.2}$$

Similarly the components h_α^i will be defined throughout the four-dimensional continuum, over the above surfaces S_3, S_2 and along the curve S_1 given by $x^1 = x^2 = x^3 = 0$ as shown by the following equations

$$\begin{array}{c|c} h_1^i = P^i(x^1, x^2, x^3, x^4) & h_2^i = Q^i(x^2, x^3, x^4) \\ [i = 1, 2, 3, 4] & \left[\begin{array}{l} i = 2, 3, 4 \\ x^1 = 0 \end{array}\right] \\ \hline h_3^i = R^i(x^3, x^4) & h_4^i = S^i(x^4) \\ \left[\begin{array}{l} i = 1, 2, 3, 4 \\ x^1 = x^2 = 0 \end{array}\right] & \left[\begin{array}{l} i = 1, 2, 3, 4 \\ x^1 = x^2 = x^3 = 0 \end{array}\right] \end{array} \tag{6.3}$$

A value $(h_2^1)_0$ will be assigned the component h_2^1 at the point P, which is now taken as the origin of the (x) coördinate system, such that the conditions $W = 0$ and $\beta \lesseqgtr 0$ are satisfied at P. It will, moreover, be assumed that the values of the h_α^i in (6.3) are such that the remainder of the normal conditions imposed in Sect. 1, namely, $W^* \gtrless 0$, $A \gtrless 0$ and $F \gtrless 0$ hold likewise at the point P; there is also the condition, which is a consequence of the underlying postulates of the space of distant parallelism, that the determinant $\left| h_i^\alpha \right| \gtrless 0$ at P.

The specification of the above data is sufficient to determine the power series expansions of the components h_α^i in the neighborhood of the point P. We observe, for example, that the quantities in the right members of (4.1) and (4.2) are known at P so that the left members of these equations are determined. Likewise the left members of (5.1) and (5.3) are determined at P since all quantities occurring in the right members of these equations are known from the assignment of the above data. In other words, all first derivatives of the quantities U, V and h_α^i are determined at the point P. To assist in the calculation of the higher derivatives of these quantities we lay down certain *rules of anteriority* which indicate the order in which these derivatives are to be determined. If $\mathfrak{A}$ and $\mathfrak{B}$ denote derivatives of U or V we shall say that $\mathfrak{A}$ is anterior to $\mathfrak{B}$ when one of the following conditions is satisfied:

(1) $\mathfrak{A}$ is of lower order than $\mathfrak{B}$;

(2) $\mathfrak{A}$ is of the same order as $\mathfrak{B}$ but involves fewer differentiations with respect to x^1;

(3) $\mathfrak{A}$ is of the same order as $\mathfrak{B}$, involves the same number of differentiations with respect to x^1, but fewer differentiations with respect to x^2;

(4) $\mathfrak{A}$ is of the same order as $\mathfrak{B}$, involves the same number of differentiations with respect to x^1 and the same number of differentiations with respect to x^2, but $\mathfrak{A}$ is a derivative of a quantity U whereas $\mathfrak{B}$ is a derivative of a quantity V.

The rules of anteriority for the derivatives of the components h_α^i can be made on the basis of the idea of the "cote" which we have previously used (footnote 4 to Note III). Let us assign "cotes" to the h_α^i and the coördinates x^α as follows:

$$\begin{array}{ll} x^\alpha & \text{has "cote" } -\alpha \\ h_2^1 & \text{has "cote" } 5 \\ h_\alpha^i & \text{has "cote" } \alpha \\ & (i \neq 1 \text{ if } \alpha = 2) \end{array}$$

Then if $\mathfrak{C}$ and $\mathfrak{D}$ denote derivatives of components h_α^i we shall say that $\mathfrak{C}$ is anterior to $\mathfrak{D}$ if:

(1) $\mathfrak{C}$ is of lower order than $\mathfrak{D}$;

(2) $\mathfrak{C}$ is of the same order as $\mathfrak{D}$ but the "cote" of $\mathfrak{C}$ is algebraically less than that of $\mathfrak{D}$.[6]

Finally we shall say that $\mathfrak{A}$ is anterior to $\mathfrak{C}$ if $\mathfrak{A}$ is of lower order than $\mathfrak{C}$ and conversely that $\mathfrak{C}$ is anterior to $\mathfrak{A}$ if $\mathfrak{C}$ is of lower order than $\mathfrak{A}$.

Now differentiate one of the equations (4.1), (4.2) or (4.3) any number of times with respect to the coördinates x^α and evaluate at the point P. The resulting equation will then express the derivative in its left member

as a sum of polynomials in anterior derivatives. In case we are dealing with an equation (4.2) the vanishing of the factor W at P prevents the occurrence in the right member of (4.2) of derivatives which are not anterior to the derivative in the left member of this equation; a similar remark applies to an equation (4.3). If we differentiate one of the equations (5.3) any number of times with respect to coördinates x^2, x^3, x^4 and evaluate at P the derivatives in the right member of the resulting equation will be anterior to the derivative in the left member. This will likewise be the case if we differentiate one of the equations (5.1) any number of times with respect to the coördinates x^α except in the case of an equation (5.1b) which involves in its right member a derivative of the component h_2^1; in this case, however, the derivative of the component h_2^1 resulting from differentiation of the equation (5.1b) can be eliminated by an obvious substitution so as to obtain an equation in which the right member contains only derivatives anterior to the derivative in its left member. From the above considerations it is obvious that any derivative of U, V or h_α^i can be determined at P when the values are known at P of all derivatives anterior to the derivative in question. It follows, therefore, that the power series expansions of the components h_α^i about the point P will be fully determined by the value $(h_2^1)_0$ of the component h_2^1 at P and the specification of data given by (6.1), (6.2) and (6.3) in accordance with the condition $|h_i^\alpha| \gtrless 0$ at P and the normal conditions in Sect. 1.

7. It was shown in Note II that the expression

$$16K(3, r + 1) + 8K(2, r + 1) \tag{7.1}$$

constituted a lower bound to the number of arbitrary derivatives of the quantities U and V of the $(r + 1)$st order; also the method explained in Sect. 4 of Note III enables us to say that there cannot be less than $4K(4, r + 2)$ derivatives of the h_α^i of order $(r + 1)$ to which arbitrary values can be assigned at the point P when the condition $W = 0$ over the surface S_3 is disregarded. When this latter condition is taken into consideration it follows, therefore, that the difference between $4K(4, r + 2)$ and $K(3, r + 1)$, or

$$4K(4, r + 1) + 3K(3, r + 1) + 4K(2, r + 1) + 4 \tag{7.2}$$

is a lower bound to the number of derivatives of the h_α^i of the $(r + 1)$st order to which arbitrary values can be assigned at the point P.

If we differentiate r times the equations (4.1), (4.2), (5.1), (5.3) and $r - 1$ times the equations (4.3), and then form the conditions of integrability of the resulting equations we obtain a system M involving the U, V and h_α^i and the derivatives of these quantities to the order $(r + 1)$ at most. Now the data specified by (6.3) shows that the number of arbitrary

derivatives of h_α^i of the $(r + 1)$st order at P is at most equal to (7.2); the number of arbitrary derivatives of U and V of the $(r + 1)$st order is easily seen to be equal to (7.1) in consequence of (6.1) and (6.2). If, therefore, one of the equations of M is not satisfied identically and if, moreover, this equation involves at least one of the derivatives of the components U, V or h_α^i of order $(r + 1)$ we shall be led to a contradiction with the fact that (7.1) or (7.2) constitutes a lower bound to the number of these derivatives which are arbitrary at the point P; in case an equation of M does not involve a derivative of U, V, or h_α^i of order $(r + 1)$ and yet is not satisfied identically we shall have a similar contradiction with regard to the lower bound for derivatives of order less than $(r + 1)$. It follows, therefore, that all conditions of integrability involved in the determination of the power series expansions of the h_α^i must be satisfied and, hence, that these expansions are unique. As the power series expansions of the h_α^i can be shown to converge within a sufficiently small neighborhood at the point P we arrive at the following[7]

EXISTENCE THEOREM. *Let us specify the functions U over the surfaces S_3 and S_3^* and also the functions V over the surface S_2 as arbitrary analytic functions of the surface coördinates represented by equations* (6.1) *and* (6.2), *respectively. Moreover, let us specify the value of the component h_2^1 at P, i.e., $x^\alpha = 0$, and also the values of the remaining components h_α^i as arbitrary analytic functions in accordance with* (6.3), *the above values being taken subject to the following conditions:*

$$W = 0, \quad |h_i^\alpha| \gtrless 0, \quad \beta \gtrless 0$$
$$W^* \gtrless 0, \quad A \gtrless 0, \quad F \gtrless 0$$

at the point P. Then there exists one, and only one, set of functions h_α^i given by convergent power series expansions about the point P, which constitutes a set of integrals of the field equations III (3.1) *and for which the surface S_3 is a characteristic.*

It should be observed that the normal conditions incorporated in the statement of the above existence theorem have been imposed merely to avoid the ambiguity which would otherwise occur in the selection of certain non-vanishing determinants formed from the coefficients of certain of the previous equations; these conditions in no way restrict the characteristic surface S_3.

8. Suppose that we confine our differentiations of the equations (4.1), (4.2), (4.3), (5.1) and (5.3) in the process of determining the power series expansions of the functions h_α^i about the point P to differentiations involving the indices x^2, x^3, x^4 alone; this is evidently possible from the rules of anteriority in Sect. 6. We then arrive at a determination of the quantities h_α^i and their first derivatives over the characteristic surface

S_3. Now if we consider the functions K in (6.1) which we can suppose to be of the form

$$\varphi_3(x^1)^3 + \varphi_4(x^1)^4 + \ldots$$

we see that this determination of the h^i_α and their first derivatives over S_3 is independent of the φ_k. Different selections of the functions $\varphi_k(x^3, x^4)$ will give different sets of integrals h^i_α of the field equations and we arrive at the fact that *there exists an infinite number of sets of integrals h^i_α of the field equations such that each set of integrals and their first derivatives assume the same values over a characteristic surface S_3.*

The above result can be extended in the following manner: Let us supplement the above process by allowing a single differentiation with respect to the coördinate x^1. Then the quantities h^i_α as well as their first and second derivatives will be determined over S_3 independently of the functions $\varphi_4, \varphi_5, \ldots$ and there is an analogous result when we restrict ourselves to $p(>1)$ differentiations with respect to the coördinate x^1. Let us say that two sets of integrals h^i_α of the field equations have contact of order C over a characteristic surface S_3 if the two sets of functions h^i_α and all their derivatives to those of order C inclusive, but not derivatives of the $(C + 1)$st order, assume the same values over S_3. We can then say that there exists an infinite number of sets of integrals h^i_α of the field equations having contact of order $C(\geqq 1)$ with one another over a characteristic surface S_3. It is important to notice that if the surface S_3 were not a characteristic the functional data common to each of these sets of integrals would be sufficient to give a unique determination of a set of integrals h^i_α of the field equations.

[1] J. Hadamard, *Lecons sur la Propagation des Ondes*, Hermann (1903), pp. 296–310.

[2] See footnote 6 to Note III.

[3] Bôcher, *Introduction to Higher Algebra*, MacMillan, p. 54 (1929).

[4] Let Q denote any determinant of order five in M_1. Assuming $J \neq 0$, we have $Q = 0$ whenever $W = 0$ by the result in the text. Hence $JQ = 0$ for $W = 0$ without restricting J to non-vanishing values. Hence $JQ \equiv WT$. Since the polynomial W is irreducible it follows from the last equation that either J or Q must involve W as a factor. But J is equal to $\alpha^2\delta^2 + \beta^2\gamma^2$ so that W is not a factor of J; hence W is a factor of Q. While the above discussion is sufficiently general to admit the possibility of J having zero values, the vanishing of J at the point P would, as a matter of fact, be in contradiction to the normal conditions in Sect. 1.

[5] See footnote 3 to Note III.

[6] A "cote" of a derivative is the integer obtained by adding to the "cote" of the function which is differentiated, the "cotes" of all the variables of differentiation, distinct or not.

[7] The proof of convergence involved here will be given later in a comprehensive exposition of the present theory.

THE LEAST AREA PROPERTY OF THE MINIMAL SURFACE DETERMINED BY AN ARBITRARY JORDAN CONTOUR

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1. In a recent paper[1] the writer gave the first solution of the problem of Plateau for an arbitrary Jordan contour, proving that if Γ is any Jordan curve in n-dimensional euclidean space there always exists a minimal surface M

$$x_i = RF_i(w), \tag{1.1}$$

$$\sum_{i=1}^{n} F_i'^2(w) = 0, \quad |w| < 1,$$

bounded by Γ.

If it is possible to span in the contour Γ at least one surface of the topological type of a circular disc having finite area, then the minimal surface M realizes the solution of the least area problem for the contour Γ: the area of M is finite and $\leqq$ the area of any continuous surface bounded by Γ.

An example was given[2] of a Jordan curve within which it is impossible to span any surface whatever of finite area, i.e., the area of every surface bounded by Γ including that of M is $+\infty$. It must not be thought, however, that the least area property of M becomes vacuous in such a case. On the contrary, the purpose of the present note is to show that there is a good sense in which this property continues to hold; this is done in the form of the following theorem.

THEOREM: *Every Jordan curve Γ in euclidean space of any number n of dimensions is the boundary of a surface M of the topological type of a circular disc having the following properties:*

(a) *M is a minimal surface, in the sense of the equations* (1.1).

(b) *If Γ' denote any continuous closed curve on M and lying altogether in its interior—the image by* (1.1) *of any Jordan curve C' whose points are all interior to the unit circle—then Γ' intercepts upon M a region whose inner area is finite and $\leqq$ the inner area of any other continuous surface bounded by Γ'.*

(c) *If the entire area of M is finite, this is $\leqq$ any other area bounded by Γ. If the area of M is $+\infty$, then the area of every continuous surface bounded by Γ is $+\infty$. The same remarks apply to the area bounded by any continuous closed curve upon M having points in common with Γ.*

It thus appears that in the case where M has infinite area the infinite part of the area lies, so to say, altogether on the edge of M.

2. Fundamental in the cited paper was the functional

$$A(g) = \frac{1}{4\pi}\int_0^{2\pi}\int_0^{2\pi} \frac{\sum_{i=1}^{n}[g_i(\theta) - g_i(\varphi)]^2}{4\sin^2\dfrac{\theta-\varphi}{2}}\,d\theta\,d\varphi,$$

where the range of the argument g consists of all parametric representations, $x_i = g_i(\theta)$, of the given contour Γ. With respect to this functional all contours divide themselves into two classes: those for which there exists a representation g such that $A(g)$ is finite, and those for which $A(g)$ is identically $+\infty$. Since it was shown that the minimum value of $A(g)$ is equal to the least area bounded by the given contour, we designated these two types as finite-area-spanning and non-finite-area-spanning, respectively. It was shown that any contour of the first type was the boundary of a minimal surface M having the least area bounded by that contour. The minimal surface M bounded by a non-finite-area-spanning contour was then obtained by considering Γ as a limit of polygons.

3. In beginning the proof of the theorem of this paper, we remark that if Γ is any finite-area-spanning contour and Γ_ρ is the analytic curve upon M corresponding by the equations (1.1) to the circle C_ρ of radius $\rho < 1$ about the origin as center, then Γ_ρ must intercept on M a smaller area than on any other continuous surface which it bounds. For if there is a surface of smaller area bounded by Γ_ρ, then by replacing the portion of M bounded by Γ_ρ by this smaller area we would have a surface of smaller area than M bounded by Γ.

4. Next, let Γ be a non-finite-area-spanning contour, represented as the limit of a sequence of polygons $\Gamma^{(m)}$. We saw in the cited paper that these polygons could be selected so that their representations minimizing $A(g)$,

$$x_i = g_i^{(m)*}(\theta), \tag{4.1}$$

tended to a representation of Γ,

$$x_i = g_i^{*}(\theta), \tag{4.2}$$

which when used in Poisson's integral,

$$x_i = RF_i(w),\ F_i(w) = \frac{1}{2\pi}\int_0^{2\pi}\frac{e^{i\theta}+w}{e^{i\theta}-w}\,g_i^{*}(\theta)d\theta, \tag{4.3}$$

gave a minimal surface M bounded by Γ. This surface is the limit of the minimal surface $M^{(m)}$ bounded by $\Gamma^{(m)}$, defined by

$$x_i = RF_i^{(m)}(w),\ F_i^{(m)}(w) = \frac{1}{2\pi}\int_0^{2\pi}\frac{e^{i\theta}+w}{e^{i\theta}-w}\,g_i^{(m)*}(\theta)d\theta. \tag{4.3$_m$}$$

M is the surface of which we assert the properties stated in our main theorem.

Let C_ρ be any circle concentric with and smaller than the unit circle and not passing through any singluar point of M; this means that at every point of C_ρ

$$\sum_{i=1}^{n} | F_i'(w) |^2 > 0. \tag{4.4}$$

Let Γ_ρ, $\Gamma_\rho^{(m)}$ be the analytic curves corresponding to C_ρ on M, $M^{(m)}$, respectively; these curves appear in definite topological representation upon C_ρ and therefore in definite point-to-point correspondence with one another. The parametric equations of Γ_ρ, $\Gamma_\rho^{(m)}$ are, respectively,

$$x_i = RF_i(\rho e^{i\theta}) = G_i(\theta), \tag{4.5}$$

$$x_i = RF_i^{(m)}(\rho e^{i\theta}) = G_i^{(m)}(\theta). \tag{4.5$_m$}$$

We have

$$A(G) = \frac{1}{4\pi} \int_0^{2\pi} \int_0^{2\pi} \frac{\sum_{i=1}^{n} [G_i(\theta) - G_i(\varphi)]^2}{4\rho^2 \sin^2 \frac{\theta - \varphi}{2}} \cdot \rho d\theta \cdot \rho d\varphi, \tag{4.6}$$

$$A(G^{(m)}) = \frac{1}{4\pi} \int_0^{2\pi} \int_0^{2\pi} \frac{\sum_{i=1}^{n} [G_i^{(m)}(\theta) - G_i^{(m)}(\varphi)]^2}{4\rho^2 \sin^2 \frac{\theta - \varphi}{2}} \cdot \rho d\theta \cdot \rho d\varphi. \tag{4.6$_m$}$$

(If we wish, we may consider the differentials of integration as $\rho d\theta$ and $\rho d\varphi$, elements of arc on C_ρ.) The integrands take for $\theta = \varphi$ the indeterminate form $\frac{0}{0}$; but it is easy to see that they have, respectively, the limiting values

$$\frac{1}{2} \sum_{i=1}^{n} | F_i'(w) |^2, \quad \frac{1}{2} \sum_{i=1}^{n} | F_i^{(m)\prime}(w) |^2, \tag{4.7}$$

for $\theta = \varphi (w = \rho e^{i\theta})$. One has only to interpret the integrand in (4.6) ((4.6$_m$)) as the square of the chord of $\Gamma_\rho(\Gamma_\rho^{(m)})$ divided by the square of the corresponding chord of C_ρ. The limit in question is evidently the square of the modulus of the conformal transformation from the circular disc to the minimal surface, and that is (4.7).

Let I denote the integrand of (4.6); with the definition (4.7) for $\theta = \varphi$, I is finite and continuous, therefore bounded, on the entire torus (θ, φ). It follows that $A(G)$, equal to *the area of M_ρ, the region of M bounded by Γ_ρ, is finite.*[3] (From the appraisal (4.10) below, which applies to I as well as I_m, it may be seen that the area of M_ρ is of the order of $(1 - \rho)^{-4}$.)

Let 2λ be the minimum value of $\frac{1}{2}\sum_{i=1}^{n} |F_i'(w)|^2$ on C_ρ; by (4.4), $2\lambda > 0$. By continuity, I stays greater than λ for values of (θ, φ) near enough to the diagonal $\theta = \varphi$ of the torus (θ, φ):

$$I > \lambda \text{ for } |\theta - \varphi| < \alpha. \tag{4.8}$$

We next prove that the integrand I_m of (4.6_m) stays uniformly bounded in θ, φ and m. Evidently, from (4.5_m) and (4.6_m),

$$I_m \leqq \frac{\sum_{i=1}^{n} |F_i^{(m)}(\rho e^{i\theta}) - F_i^{(m)}(\rho e^{i\varphi})|^2}{4\rho^2 \sin^2 \frac{\theta - \varphi}{2}}. \tag{4.9}$$

From (4.4),

$$F_i^{(m)}(\rho e^{i\theta}) - F_i^{(m)}(\rho e^{i\varphi}) = \frac{1}{\pi}\int_0^{2\pi} \frac{e^{i\omega}(\rho e^{i\theta} - \rho e^{i\varphi})}{(e^{i\omega} - \rho e^{i\theta})(e^{i\omega} - \rho e^{i\varphi})} g_i^{(m)*}(\omega) d\omega,$$

whence

$$\frac{|F_i^{(m)}(\rho e^{i\theta}) - F_i^{(m)}(\rho e^{i\varphi})|}{2\rho \sin \frac{\theta - \varphi}{2}} = \left| \frac{1}{\pi}\int_0^{2\pi} \frac{e^{i\omega}}{(e^{i\omega} - \rho e^{i\theta})(e^{i\omega} - \rho e^{i\varphi})} g_i^{(m)*}(\omega) d\omega \right|$$

since

$$|\rho e^{i\theta} - \rho e^{i\varphi}| = 2\rho \sin \frac{\theta - \varphi}{2}.$$

Obviously all the contours $\Gamma^{(m)}$ can be comprised in a cube of edge $2R$ with center at the origin; therefore

$$\frac{|F_i^{(m)}(\rho e^{i\theta}) - F_i^{(m)}(\rho e^{i\varphi})|}{2\rho \sin \frac{\theta - \varphi}{2}} \leqq \frac{2R}{(1 - \rho)^2},$$

and consequently, by (4.9),

$$I_m \leqq \frac{4nR^2}{(1 - \rho)^4}. \tag{4.10}$$

Since I_m thus stays uniformly bounded as it approaches to I, it follows that

$$\lim_{m \to \infty} A(G^{(m)}) = A(G). \tag{4.11}$$

By (4.8) and (4.10) we have that

$$\frac{I_m}{I} < B \text{ for } 0 < |\theta - \varphi| < \alpha, \tag{4.12}$$

B and α being independent of m.

The above is preliminary to the proof of the assertion that $A(G)$ *is the least value of the A-functional for the contour* Γ_ρ. Suppose, on the contrary, that G^* is a parametric representation of Γ_ρ such that

$$A(G^*) < A(G). \tag{4.13}$$

G^* is derivable from G by a parameter transformation on Γ_ρ; let $G^{(m)*}$ be the representation of $\Gamma_\rho^{(m)}$ derived from $G^{(m)}$ by the same parameter transformation. The quotient $\frac{I_m}{I}$ in (4.12) is evidently the ratio of the squares of corresponding chords of $\Gamma_\rho^{(m)}$ and Γ_ρ, and corresponding chords remain such after the same parameter transformation is effected on both contours. It follows that, in an obvious notation,

$$\frac{I_m^*}{I^*} = \frac{I_m}{I} < B \text{ for } 0 < |\theta - \varphi| < \alpha, \tag{4.14}$$

B and α being the same as in (4.12).

Now $A(G)$ being finite, so also is $A(G^*)$, and therefore

$$A_\epsilon(G^*) = \frac{1}{4\pi} \int\int_{T_\epsilon} I^* . \rho d\theta . \rho d\varphi \tag{4.15}$$

—where T_ϵ is the domain (θ, φ) where $|\theta - \varphi| \geqq \epsilon$—converges to the finite limit $A(G^*)$ for $\epsilon \longrightarrow 0$. It follows by (4.14) that

$$A_\epsilon(G^{(m)*}) = \frac{1}{4\pi} \int\int_{T_\epsilon} I_m^* . \rho d\theta . \rho d\varphi \tag{4.16}$$

converges *uniformly* to $A(G^{(m)*})$ for $\epsilon \longrightarrow 0$.

Now since I_m^* stays uniformly bounded on T_ϵ in θ, φ and m, in fact

$$I_m^* \leqq \frac{4nR^2}{4\rho^2 \sin^2 \frac{\epsilon}{2}},$$

and furthermore

$$\lim_{m \to \infty} I_m^* = I^*,$$

we have

$$\lim_{m \to \infty} A_\epsilon(G^{(m)*}) = A_\epsilon(G^*);$$

hence

$$\lim_{\epsilon \to 0} \lim_{m \to \infty} A_\epsilon(G^{(m)*}) = \lim_{\epsilon \to 0} A_\epsilon(G^*). \tag{4.17}$$

On account of the uniformity of approach of $A_\epsilon(G^{(m)*})$ to $A(G^{(m)*})$ when $\epsilon \longrightarrow 0$, it is permissible by a well-known mode of reasoning to interchange the order of the limiting processes on the left of (4.17), and we find

$$\lim_{m \to \infty} A(G^{(m)*}) = A(G^*). \tag{4.18}$$

By combining the relations (4.11), (4.13) and (4.18), we see readily that for sufficiently large values of m

$$A(G^{(m)*}) < A(G^{(m)}); \tag{4.19}$$

but this contradicts the fact, proved in §3, that $A(G^{(m)})$ is the minimum value of the A-functional for $\Gamma_\rho^{(m)}$, this being the same as the minimum area bounded by $\Gamma_\rho^{(m)}$.[3]

From the fact, now proved, that $A(G)$ is the minimum value of the A-functional for the contour Γ_ρ, it follows by the relations between the A-functional and area[3] that *the area of* $M_\rho \leqq$ *that of any other continuous surface bounded by* Γ_ρ.

5. Let now Γ' denote an arbitrary continuous closed curve in the interior of M, the image of any Jordan curve C' in the interior of the circular disc $|w| < 1$. On account of the fact that the singular points of M, where

$$\sum_{i=1}^{n} |F_i'(w)|^2 = 0,$$

have no point of condensation in the interior of $|w| < 1$, we can construct with the origin as center a circle C_ρ of radius $\rho < 1$ having on its circumference no singular points and containing C' in its interior.

Denote by M' the region of M_ρ interior to Γ'; if M' is not the surface of least area bounded by Γ', let M'^* be this surface, whose existence is assured by the writer's earlier paper. Then by replacing M' by M'^* we would have a surface bounded by Γ_ρ with an area less than that of M_ρ, which is contrary to the result stated at the end of §4.

[1] "Solution of the Problem of Plateau," *Trans. Amer. Math. Soc.*, **33**, No. 1 (Jan., 1931), pp. 263–321.

[2] Loc. cit., §27.

[3] For the relations between the A-functional and area see the cited paper, §§ 22–26.

FUNCTION SPACE-TIME MANIFOLDS

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1. *Composite Geometries.*[1]—A theory of functional geometries and their functional invariants has been developed by me in several publications.[2] More recently I undertook the task of extending some of the results to composite geometries[3] in which a point has coördinates $(y^x, y^1, y^2, \ldots, y^n)$, where y^x is a continuous function of x defined over the fundamental interval (a, b).

It is convenient to adopt at the outset the following conventions:

(A) Any Latin index will have the discrete integral range $1, 2, \ldots, n$. A repeated Latin index, in a term will denote summation with respect to that index over $1, 2, \ldots, n$.

(B) Any Greek index $\alpha\beta\ldots\xi 0$ will have the continuous range of the fundamental interval (a, b). A repetition of such a Greek index, in a term will denote Riemann integration with respect to that index over the interval (a, b).

(C) Any Greek index $\pi\rho\ldots\psi\omega$ will have the composite range consisting of the discrete and continuous ranges of (A) and (B), respectively. A repetition of such a Greek index in a term will denote a composite functional operation that consists of a summation over the discrete range and a Riemann integration over the continuous range.

(D) A parenthesis around any repeated index (Latin or Greek) will denote that that index is to be kept free and is not to be subjected to the functional operation appropriate to the case.

Consider the uniquely reversible functional transformations

$$\bar{y}^\sigma = f^\sigma[y^\tau] \tag{1.1}$$

in our composite space. The differentials in the Fréchét sense (with max. $|y_1^\tau - y_2^\tau|$ as the "metric") are assumed to be of the form

$$\delta\bar{y}^\sigma = p^\sigma\delta y^\sigma + p^\sigma_\tau\delta y^\tau \quad (p^\sigma = 0, p^\alpha \neq 0) \tag{1.2}$$

The bordered Fredholm determinant[4]

$$D\begin{bmatrix} p^\alpha_\beta/p^{(\beta)} & , & p^\alpha_b \\ p^a_\beta/p^{(\beta)} & , & p^a_b \end{bmatrix} \tag{1.3}$$

is assumed not to vanish.

The contravariant vector law of transformation is given by formula (1.2) while the covariant vector law of transformation is given by

$$\xi_\sigma[y^\tau] = \bar{\xi}_\sigma[\bar{y}^\tau]\, p^{(\sigma)} + \bar{\xi}, p^\tau_\sigma \tag{1.4}$$

If our composite space possesses an affine connection, then the covariant differential $D\xi^\rho$ of a contravariant vector $\xi^\rho[y^\sigma]$ is given by

$$\left.\begin{aligned} D\xi^\rho = {} & \delta\xi^\rho + L^\rho_{\sigma\tau}\xi^\sigma\delta y^\tau + M^\rho_\sigma\xi^\sigma\delta y^\sigma \\ & + N^\rho_\sigma\xi^\rho\delta y^\sigma + O^\rho_\sigma\xi^\sigma\delta y^\rho + P^\rho\xi^\rho\delta y^\rho \end{aligned}\right\} \tag{1.5}$$

subject to the invariant conditions[5]

$$M^\rho_b = N^a_b = P^a = 0. \tag{1.6}$$

For the symmetric affine connection we also have

$$O^a_b = 0 \tag{1.7}$$

as a *consequence* of $N^a_b = 0$.

An important special case of the above is furnished by "Riemannian" composite spaces. The analogues of the Christoffel symbols of the second kind are given by the symmetric affine connection that is based on the quadratic differential form in the composite space

$$g_{\sigma\tau}[y^\pi]\delta y^\sigma\delta y^\tau + g_\sigma[y^\pi](\delta y^\sigma)^2 \ (g_{\sigma\tau} = g_{\tau\sigma}\ ,\ g_a = 0\ ,\ g_\alpha \neq 0). \tag{1.8}$$

To develop certain important portions of a "Riemannian" composite geometry we must restrict ourselves to the forms (1.8) for which the bordered Fredholm determinant

$$D\begin{bmatrix} g_{\alpha\beta}/g_\beta\ ,\ g_{\alpha b} \\ g_{a\beta}/g_\beta\ ,\ g_{ab} \end{bmatrix}$$

does not vanish.

The $\infty + n$ absolute linear forms

$$\xi^{(\sigma)}[y]\,\eta_\sigma[y] + \xi^\pi_\sigma[y]\eta_\pi[y] \ (\xi^a = 0,\ \xi^\alpha \neq 0)$$

in the covariant vector η_π define an $\infty + n$ family of contravariant vectors ξ^σ, ξ^π_σ. A geometry with teleparallelism (distant parallelism) can be developed by requiring that the bordered Fredholm determinant

$$D\begin{bmatrix} \xi^\alpha_\beta/\xi^{(\beta)}\ ,\ \xi^\alpha_b \\ \xi^a_\beta/\xi^{(\beta)}\ ,\ \xi^a_b \end{bmatrix}$$

is different from zero.

The case $n = 1$ is of special interest in all the above considerations. If we identify the coördinate y^1 with the time t we obtain an $\infty + 1$ dimensional manifold with coördinates (y^α, t). We shall use the terminology *function space-time manifolds* for such manifolds. We shall also use this phraseology even when the coördinate t is not identified with the time.

2. *Integral Invariants in Function Space.*[6]—The remaining part of the

paper will be devoted to some special invariant theoretic problems in function space-time manifolds. No hypothesis will be made as to the existence of an affine connection. Before we proceed with these invariant problems we must consider some preliminary theorems in the function space whose points have coördinates $(y_1^\alpha, y_2^\alpha, \ldots, y_n^\alpha)$, where $y_1^\alpha, \ldots, y_n^\alpha$ are n continuous functions of the continuous variable α defined in the fundamental interval (a, b).

Consider the linear functional differential form

$$A_\alpha^i[y]\delta y_i^\alpha. \tag{2.1}$$

The functional arguments of the n functionals A_α^i are the n functions y_j^α. We shall assume that the A_α^i are analytic functions of a parameter t, whenever the n functions y_j^α are analytic in the same parameter t. Furthermore we shall assume that the differentials of A_α^i (in the Fréchét sense) are of the form

$$\delta A_\alpha^i = {}_{y_j^\alpha}A_\alpha^i \delta y_j^{(\alpha)} + A_{\alpha,y_j^\beta}^i \delta y_j^\beta, \tag{2.2}$$

Similar restrictions are to be made on all the functionals considered throughout the paper. From the properties of the Fréchét differentials it follows that

$$\frac{\partial A_\alpha^i}{\partial t} = {}_{y_j^\alpha}A_\alpha^i \frac{\partial y_j^{(\alpha)}}{\partial t} + A_{\alpha,y_j^\beta}^i \frac{\partial y_j^\beta}{\partial t}. \tag{2.3}$$

DEFINITION. *A functional form F in the differentials $\delta_1 y_j^\alpha, \delta_2 y_j^\alpha, \ldots, \delta_r y_j^\alpha$ will be said to be an invariant of the integro-differential system*

$$\frac{\partial y_i^\alpha(t)}{\partial t} = f_i^\alpha[y] \tag{2.4}$$

if the $\dfrac{\partial F}{\partial t}$ *along the functional trajectories of* (2.4) *vanishes identically in* $\delta_1 y_j^\alpha, \ldots, \delta_r y_j^\alpha$. *A form F will be said to be an invariant attached to the functional trajectories of* (2.4) *if the above invariance holds for the infinitude of systems*

$$\frac{\partial y_i^\alpha(t)}{\partial t} = \rho[y] f_i^\alpha[y] \tag{2.5}$$

obtained by taking $\rho[y]$ to be an arbitrary scalar functional of $y_1^\alpha, \ldots, y_n^\alpha$.

THEOREM I. *A necessary and sufficient condition that the functional form*

$$A_\alpha^i[y]\delta y_i^\alpha \tag{2.6}$$

be an invariant of the integro-differential system (2.4) *is that the n-functionals $A_\alpha^1[y], \ldots, A_\alpha^n[y]$ satisfy the following system of functional equations with functional derivatives*

$$(_{y_j^\alpha},A_\alpha^i - _{y_i^\alpha},A_\alpha^j)f_j^{(\alpha)} + (A_{\alpha,y_j^\beta}^i - A_{\beta,y_i^\alpha}^j)f_j^\beta + (A_\beta^j f_j^\beta)_{,y_i^\alpha} = 0. \quad (2.7)$$

A necessary and sufficient condition that (2.6) *be an invariant attached to the functional trajectories of* (2.4) *is that the* A_α^i *functionals satisfy the system of functional equations*

$$\left.\begin{aligned}(_{y_j^\alpha}, A_\alpha^i - _{y_i^\alpha}, A_\alpha^j)f_j^{(\alpha)} + (A_{\alpha,y_j^\beta}^i - A_{\beta,y_i^\alpha}^j)f_j^\beta\,\alpha = 0\\ A_\beta^j f_j^\beta = 0.\end{aligned}\right\} \quad (2.8)$$

Since

$$\delta f_i^\alpha = _{y_j^\alpha},f_i^{(\alpha)}\delta y_j^\alpha + f_{i,y_j^\beta}^\alpha \delta y_j^\beta \quad (2.9)$$

it follows that

$$\frac{\partial(\delta y_i^\alpha)}{\partial t} = _{y_j^\alpha},f_i^{(\alpha)}\delta y_j^\alpha + f_{i,y_j^\beta}^\alpha \delta y_j^\beta. \quad (2.10)$$

With the aid of (2.3), (2.4), (2.10) we obtain after some calculation and rearrangement the following conditions for invariance

$$(A_{\alpha,y_j^\beta}^i - A_{\beta,y_i^\alpha}^j)f_j^\beta \delta y_i^\alpha + (_{y_j^\alpha},A_\alpha^i - _{y_i^\alpha},A_\alpha^j)f_j^\alpha \delta y_i^\alpha + \delta(A_\beta^j f_j^\beta) = 0 \quad (2.11)$$

identically in the arbitrary functions δy_i^α. An application of an obvious extension of a known theorem shows that (2.7) implies and is implied by (2.11). The second part of the theorem follows quite simply. On making use of the arbitrariness of the functional ρ we obtain conditions (2.11) together with the condition

$$A_\beta^j f_j^\beta = 0. \quad (2.17)$$

But (2.11) together with (2.17) is completely equivalent to the functional equations (2.8).

Q. E. D.

From an alternating bilinear form

$$\omega_{\delta_1\delta_2} = A_\alpha^{ij}\delta_1 y_i^\alpha \delta_2 y_j^\alpha + A_{\alpha\beta}^{ij}\delta_1 y_i^\alpha \delta_2 y_j^\beta \; (A_\alpha^{ij} = -A_\alpha^{ji}, A_{\alpha\beta}^{ij} = -A_{\beta\alpha}^{ji}) \quad (2.18)$$

we can form the trilinear form

$$\omega_{\delta_1\delta_2\delta_3} = \delta_3\omega_{\delta_1\delta_2} - \delta_1\omega_{\delta_2\delta_3} - \delta_2\omega_{\delta_1\delta_3}. \quad (2.19)$$

By calculation we obtain

$$\left.\begin{aligned}\omega_{\delta_1\delta_2\delta_3} = {} & B_\alpha^{ijk}\delta_1 y_i^\alpha \delta_2 y_j^\alpha \delta_3 y_k^\alpha + C_{\alpha\beta}^{ijk}\delta_1 y_i^\alpha \delta_2 y_j^\alpha \delta_3 y_k^\beta\\ & + D_{\alpha\beta}^{ijk}\delta_1 y_i^\alpha \delta_2 y_j^\beta \delta_3 y_k^\alpha + E_{\alpha\beta}^{ijk}\delta_1 y_i^\alpha \delta_2 y_j^\beta \delta_3 y_k^\beta\\ & + F_{\alpha\beta\gamma}^{ijk}\delta_1 y_i^\alpha \delta_2 y_j^\beta \delta_3 y_k^\gamma,\end{aligned}\right\} \quad (2.20)$$

where

$$\left.\begin{aligned} B^{ijk}_{\alpha} &= {}_{y^\alpha_k},A^{ij}_{\alpha} - {}_{y^\alpha_i},A^{kj}_{\alpha} - {}_{y^\alpha_j},A^{ik}_{\alpha} \\ C^{ijk}_{\alpha\beta} &= A^{ij}_{\alpha\,,y^\beta_k} - {}_{y^\alpha_i},A^{kj}_{\beta\alpha} - {}_{y^\alpha_j},A^{ik}_{\alpha\beta} \\ D^{ijk}_{\alpha\beta} &= {}_{y^\alpha_k},A^{ij}_{\alpha\beta} - {}_{y^\alpha_i},A^{kj}_{\alpha\beta} - A^{ik}_{\alpha\,,y^\beta_j} \\ E^{ijk}_{\alpha\beta} &= {}_{y^\beta_k},A^{ij}_{\alpha\beta} - A^{kj}_{\beta\,,y^\alpha_i} - {}_{y^\beta_j},A^{ik}_{\alpha\beta} \\ F^{ijk}_{\alpha\beta\gamma} &= A^{ij}_{\alpha\beta,y^\gamma_k} - A^{kj}_{\gamma\beta,y^\alpha_i} - A^{ik}_{\alpha\gamma,y^\beta_j}. \end{aligned}\right\} \tag{2.21}$$

We need the explicit expression of these results in the conditions of the following theorem.

THEOREM II. *A necessary and sufficient condition that the alternating functional form* (2.18) *be an invariant of the integro-differential system* (2.4) *is that the functionals* A^{ij}_{α} *and* $A^{ij}_{\alpha\beta}$ *satisfy the system of functional equations.*

$$\left.\begin{aligned} B^{ijk}_{\alpha} f^{(\alpha)}_k + C^{ijk}_{\alpha\sigma} f^{\sigma}_k + G^{ij}_{\alpha} &= 0 \\ D^{ijk}_{\alpha\beta} f^{(\alpha)}_k + E^{ijk}_{\alpha\beta} f^{(\beta)}_k + F^{ijk}_{\alpha\beta\gamma} f^{\gamma}_k + H^{ji}_{\alpha\beta} &= 0, \end{aligned}\right\} \tag{2.22}$$

where the functionals B, C, D, E, F are defined in (2.21) *and*

$$\left.\begin{aligned} G^{ij}_{\alpha} &= {}_{y^\alpha_j},(A^{ik}_{\alpha} f^{(\alpha)}_k + A^{ik}_{\alpha\sigma} f^{\sigma}_k) - {}_{y^\alpha_i},(A^{jk}_{\alpha} f^{(\alpha)}_k + A^{jk}_{\alpha\sigma} f^{\sigma}_k) \\ H^{ij}_{\alpha\beta} &= (A^{ik}_{\alpha} f^{(\alpha)}_k + A^{ik}_{\alpha\sigma} f^{\sigma}_k)_{,y^\beta_j} - (A^{jk}_{\beta} f^{(\beta)}_k + A^{jk}_{\beta\sigma} f^{\sigma}_k)_{,y^\alpha_i} \end{aligned}\right\} \tag{2.23}$$

A necessary and sufficient condition that (2.18) *be an invariant attached to the functional trajectories of* (2.4) *is that* A^{ij}_{α} *and* $A^{ij}_{\alpha\beta}$ *satisfy the functional equations*

$$\left.\begin{aligned} B^{ijk}_{\alpha} f^{(\alpha)}_k + C^{ijk}_{\alpha\sigma} f^{\sigma}_k &= 0 \\ D^{ijk}_{\alpha\beta} f^{(\alpha)}_k + E^{ijk}_{\alpha\beta} f^{(\beta)}_k + F^{ijk}_{\alpha\beta\gamma} f^{\gamma}_k &= 0 \\ A^{ij}_{\alpha} f^{(\alpha)}_j + A^{ij}_{\alpha\sigma} f^{\sigma}_j &= 0. \end{aligned}\right\} \tag{2.24}$$

3. *Integral Invariants in Function Space-Time.*[6]—The system of equations

$$\frac{\partial y^\alpha_j}{\partial \tau} = f^\alpha_j [y, t], \frac{\partial t}{\partial \tau} = f[y, t] \tag{3.1}$$

in function space-time manifolds includes as a special case the system

$$\frac{\partial y^\alpha_j}{\partial \tau} = f^\alpha_i [y], \frac{\partial t}{\partial \tau} = 1. \tag{3.2}$$

THEOREM III. *A necessary and sufficient condition that the linear form*

$$A^i_\alpha [y]\delta y^\alpha_i + A[y]\delta t \tag{3.3}$$

be an invariant of (3.2) *is that*

$$A^i_\alpha \delta y^\alpha_i$$

be an invariant of (2.4) *and that* $A[y]$ *be a scalar functional invariant of* (2.4). *A necessary and sufficient condition that the alternating bilinear form*

$$\left.\begin{aligned} &A^{ij}_{\alpha}\,\delta_1 y^{\alpha}_i\,\delta_2 y^{\alpha}_j + A^{ij}_{\alpha\beta}\,\delta_1 y^{\alpha}_i\,\delta_2 y^{\beta}_j + A^{i}_{\alpha}\,\delta_1 y^{\alpha}_i\,\delta_2 t - A^{i}_{\alpha}\,\delta_1 t\,\delta_2 y^{\alpha}_i \\ &(A^{ij}_{\alpha} = -A^{ji}_{\alpha},\ A^{ij}_{\alpha\beta} = -A^{ji}_{\beta\alpha}) \end{aligned}\right\} \tag{3.4}$$

be an invariant of (3.2) *is that both* (2.18) *and* (2.6) *be invariants of* (2.4).

The reader can supply without much difficulty the proof for the first part of the theorem. To prove the second part one has to verify first that

$$\left.\begin{aligned} &\frac{\partial}{\partial\tau}\,(A^{i}_{\alpha}\,\delta_1 t\,\delta_2 y^{\alpha}_i) = [(A^{i}_{\alpha,y^{\beta}_j} - A^{j}_{\beta,y^{\alpha}_i})f^{\beta}_j \\ &+ (_{y^{\alpha}_j}, A^{i}_{\alpha} - {}_{y^{\alpha}_i}, A^{j}_{\alpha})f^{\alpha}_j + (A^{j}_{\beta}f^{\beta}_j)_{,y^{\alpha}_i}]\delta_1 t\,\delta_2 y^{\alpha}_i \end{aligned}\right\}. \tag{3.5}$$

By Theorem I it follows that the vanishing of the bracket terms in (3.5) constitutes the condition for the invariance of $A^{i}_{\alpha}\delta y^{\alpha}_i$. The invariance of (2.18) follows with the aid of Theorem II.

THEOREM IV. *A necessary and sufficient condition that* (3.4) *be an invariant attached to the functional trajectories of* (3.2) *is that the bilinear form* (2.18) *be an invariant of* (2.4) *and that the functionals* A^{i}_{α} *be given by*

$$A^{i}_{\alpha} = -(A^{ik}_{\alpha}f^{(\alpha)}_k + A^{ik}_{\alpha\sigma}f^{\sigma}_k). \tag{3.6}$$

The proof differs from that of the preceding theorem in that

$$\frac{\partial(\delta t)}{\partial\tau} = \delta\rho,$$

where ρ is an arbitrary scalar functional. On performing the usual calculations appropriate to the case on hand and then making use of the arbitrariness of ρ, we obtain the conditions (2.22), (2.7), (3.6) and

$$A^{j}_{\beta}f^{\beta}_j = 0. \tag{3.7}$$

But (3.7) is satisfied identically in virtue of (3.6) and the identities satisfied by A^{ik}_{α} and $A^{ik}_{\alpha\beta}$. An obvious application of Theorem III completes the proof of our theorem.

Definition.—A linear functional form ω_δ will be said to be a relative invariant (attached or unattached) of the integro-differential system appropriate to the case, whenever the alternating form (bilinear covariant $\delta_2\omega_{\delta_1} - \delta_1\omega_{\delta_2}$ is an invariant (attached or unattached) of the same integro-differential system.

THEOREM V. *A necessary and sufficient condition that the linear form*

$$B^{i}_{\alpha}[y]\,\delta y^{\alpha}_i + B[y]\,\delta t \tag{3.8}$$

be a relative invariant of the system (3.2) *is that*

$$B^i_\alpha [y]\, \delta y^\alpha_i \tag{3.9}$$

be a relative invariant of

$$\frac{\partial y^\alpha_i}{\partial t} = f^\alpha_i [y] \tag{3.10}$$

and that the functional $B[y]$ *satisfy the functional equation*

$$\left(B_{,y^\beta_j} f^\beta_j\right)_{,y^\alpha_i} = 0. \tag{3.11}$$

The bilinear covariant of (3.8) is given by

$$A^{ij}_\alpha\, \delta_1 y^\alpha_i\, \delta_2 y^\beta_j + A^{ij}_{\alpha\beta}\, \delta_1 y^\alpha_i\, \delta_2 y^\beta_j + A^i_\alpha\, \delta_1 y^\alpha_i\, \delta_2 t - A^i_\alpha\, \delta_1 t\, \delta_2 y^\alpha_i, \tag{3.12}$$

where

$$\left.\begin{aligned} A^{ij}_\alpha &= {}_{,y^\alpha_j} B^i_\alpha - {}_{,y^\alpha_i} B^j_\alpha \\ A^{ij}_{\alpha\beta} &= B^i_{\alpha,y^\beta_j} - B^j_{\beta,y^\alpha_i} \\ A^i_\alpha &= -B_{,y^\alpha_i} \end{aligned}\right\} \tag{3.13}$$

The functionals B^{ijk}_α, $C^{ijk}_{\alpha\sigma}$, $D^{ijk}_{\alpha\beta}$, $E^{ijk}_{\alpha\beta}$, $F^{ijk}_{\alpha\beta}$, $\left({}_{,y^\alpha_j} A^i_\alpha - {}_{,y^\alpha_i} A^j_\alpha\right)$, $\left(A^i_{\alpha,y^\beta_j} - A^j_{\beta,y^\alpha_i}\right)$ when calculated on the basis of (3.13) all vanish identically. Hence the conditions for the relative invariance of (3.8) under the system (3.2) reduce to the following set of functional equations

$$\left.\begin{aligned} &G^{ij}_\alpha = 0,\ H^{ij}_{\alpha\beta} = 0 \\ &(A^j_\beta f^\beta_j)_{,y^\alpha_i} = 0. \end{aligned}\right\} \tag{3.14}$$

We understand that G^{ij}_α, $H^{ij}_{\alpha\beta}$, A^j_β in (3.14) are calculated on the basis of the definitions (3.13). With the aid of Theorem II one can verify that the equations

$$G^{ij}_\alpha = 0,\ H^{ij}_{\alpha\beta} = 0 \tag{3.15}$$

are the necessary and sufficient conditions for the relative invariance of

$$B^i_\alpha\, \delta y^\alpha_i \tag{3.16}$$

under the system (3.10). The truth of our theorem follows then immediately.

THEOREM VI. *A necessary and sufficient condition that the linear form* (3.8) *in function space-time be a relative invariant attached to the functional trajectories of the integro-differential system* (3.2) *is that* (3.16) *be a relative*

invariant of the system (3.10) *and that the functional* $B[y]$ *satisfy the functional equation*

$$B_{,y_i^\alpha} = \left(_{,y_k^\alpha}B_\alpha^i - {}_{,y_i^\alpha}B_\alpha^k\right) f_k^{(\alpha)} + \left(B_{\alpha,y_k^\sigma}^i - B_{\alpha,y_i^\sigma}^k\right) f_k^\sigma. \qquad (3.17)$$

With the aid of Theorems IV and V, we obtain the conditions (3.14) together with (3.17). From the form of (3.17), we see that

$$B_{,y_i^\alpha} f_i^\alpha = 0. \qquad (3.18)$$

Hence the equation

$$(A_\beta^j f_j^\beta)_{,y_i^\alpha} = 0$$

is automatically satisfied in virtue of (3.17). This means that (3.15) together with (3.17) constitute the necessary and sufficient conditions.

COROLLARY. *The necessary and sufficient conditions of Theorem VI are equivalent to the following*:

(1) *the functional equations* (3.17) *are completely integrable*

(2) $B[y]$ *satisfies the equations* (3.17).

This can be verified by observing that the conditions (3.15) are the conditions for the complete integrability of the equations (3.17) with $B[y]$ as the unknown.

A simple example of such a relative invariant is given by

$$p_\alpha \delta q^\alpha - H[q, p]\, \delta t. \qquad (3.19)$$

This functional form is a relative invariant attached to the trajectories of the integro-differential system[7]

$$\frac{\partial q^\alpha(\tau)}{\partial \tau} = H_{,p_\alpha}, \quad \frac{\partial p_\alpha(\tau)}{\partial \tau} = -H_{,q\alpha}, \quad \frac{\partial t}{\partial \tau} = 1.$$

[1] A more detailed account of the results of this paragraph will be published elsewhere in Part III of an extended memoir entitled, "Functional Geometries and Their Functional Invariants."

[2] A. D. Michal, *Amer. J. Math.*, **50**, 473–517 (1928) (presented to the *Amer. Math. Soc.* at the New York meeting, October, 1927); these PROCEEDINGS, **16**, 88–94, 162–164, 165–168 (1930).

[3] Cf. the abstract in the *Bull. Amer. Math. Soc.*, **36**, 485 (1930).

[4] A. D. Michal and L. S. Kennison, these PROCEEDINGS, **16**, 617–619 (1930).

[5] The conditions (1.6) insure the unicity of the functional expansions in (1.5). Of course, we understand here and throughout our paper that all functionals are continuous as functions of the continuous variables on which they depend in particular in addition to their being continuous as functionals of their functional arguments.

[6] Compare some of the results of this paragraph with my n-dimensional investigations. See my paper in the *Trans. Amer Math. Soc.*, **29**, 612–646 (1927). For the general subject of integral invariants in n-dimensions the reader is referred to the

excellent papers and books of H. Poincaré, S Lie, E. Goursat, E. Cartan and Th. De Donder. For a good bibliography up to 1927, see Th. De Donder, "*Théorie des Invariants Intégraux*" (1927).

[7] Vito Volterra was the first to consider the analogues in function space of the Hamilton canonical equations. See his paper, "Equazioni integro-differenziali ed equazioni alle derivate funzionali," *R. Acc. dei Lincei Rend.*, **23** (1914).

THE COMPOSITION OF THE INTERIOR OF THE EARTH

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As is well known, the density of the earth's crust is about 2.7, while the density of the whole earth is 5.52 gms./cc. This difference is usually explained by the hypothesis that the interior of the earth is composed of heavy metals, chiefly of iron.[1] It is assumed that the heavy elements have fallen to the interior during the formative stages of the earth and stayed there.[2] This theory is, however, open to very serious objections. The iron core theory would require that about 46% of the mass of the earth consisted of iron and other heavy elements. It is difficult to believe that the composition of the earth is totally different from that of other stellar bodies. The spectroscopic examination of stars[3] and the evidence offered by the meteorites seem to show that iron forms a small part of the bulk of the stars, and while the abundance of the elements seems to be roughly the same in stars and meteorites as in the crust of the earth on the iron core theory,[4] there is complete disagreement so far as the iron and oxygen content is concerned, as the following table shows:

TABLE 1

	CRUST	STARS	METEORITES	WHOLE EARTH
Oxygen	55	50	54	35
Hydrogen	16	5	0	8
Silicon	16	6	0	9.5
Iron	1.5	2	13	46.3

Even if we assume that the spectroscopic data for iron are not complete and that the percentage weight should be multiplied by a factor of 4 or 5, iron would still form a very much smaller portion of the universe than the percentage for the earth demanded by the iron core theory.

Also, if the heavier elements are expected to sink to the interior of the planet we would expect the heavier elements of the sun to be concentrated at the center, and the surface would then consist of the lighter ones. On the planetesimal theory of the origin of the earth the tides, which were responsible for the formation of the earth from the sun consisted chiefly

of the outer and lighter portion of the sun. The earth forming a very small part of the sun was probably the result of the condensation of the outer and lighter layers, and there would be very little iron in its bulk.

The hypothesis that the heavier elements of the earth sank into the interior of the planet is in itself open to objection, for this would require that all heavy elements including the radioactive ones would be more abundant in the interior than in the crust. Jeffrey has shown,[5] however, that a distribution of radioactive elements throughout the earth no greater in abundance than in the crust would prevent the earth from cooling, because of the heat liberated in the process of radioactivity.

Also, on the basis of probability the abundance of elements in the crust would be proportional, approximately, to n/d, where n is the total number of atoms of a given element present, and d is its density. On this basis one would expect iron to be at least as abundant in the crust as silicon, if the iron core theory is correct. Actually there are more than ten atoms of silicon in the crust of the earth for each atom of iron.

The foregoing considerations lead one to believe that the iron core theory is not very plausible, and other hypotheses have to be made in order to explain the high density of the earth.

The object of this paper is to present a theory explaining the high density of the interior of the earth on the basis of the ionization of the elements composing the core. The composition of the earth is assumed to be no different from that shown by other celestial bodies.

Any theory concerning the composition of the earth must satisfy the following conditions. In the first place, the theory must account for the total mass of the earth, in agreement with that observed from experiments on the gravitational constant. In the second place, the distribution of mass must be such as to give the moment of inertia in agreement with the value deduced from the known precessional constants of the earth. In addition, the manner in which seismic disturbances are propagated lead one to believe that the earth consists of two distinct layers, the upper, behaving like a rigid body, while the lower must consist of material in liquid form, inasmuch as seismic disturbances seem to be absorbed by that part of the earth. We may, therefore, assume that there is a core of radius r and of density ρ, and an envelope of thickness $R-r$, where R is the radius of the earth, and of density ρ_2. The first two conditions mentioned above give rise to two equations, one for the mass of the earth and the other for its moment of inertia.

$$r^3\rho_1 + (R^3 - r^3)\rho_2 = 5.52R^3 \qquad (1)$$

$$r_1^5\rho_1 + (R^5 - r_1^5)\rho_2 = 4.43R^5 \qquad (2)$$

We have two equations with three unknowns. The third relation

between the variables may be obtained from the following considerations. As is well known the temperature near the surface of the earth rises approximately one degree C. for each 100 feet increase in depth. If this gradient prevails for large distances below the surface of the earth the temperature would soon reach a level at which decomposition or dissociation of molecules takes place, and the more volatile of the elements composing the molecules would be driven off and form an envelope around elements which are solid at ordinary temperatures. The envelope would, on this view, consist of the present crust together with most of the permanent gases contained in the earth, all other elements forming the core. If we assume that the composition of the earth as a whole is no different from that of the crust or of the upper layers of the sun, the gases, together with the crust, would form about 70% of the material of the earth and the core would make up about 30% of the mass of the earth, and we have the third relation:

$$r_1^3\rho_1 = 1.66\,R^3.$$

The simultaneous solution of the three equations gives the following values for the unknowns: $\rho_1 = 15$, $\rho_2 = 4.2$, $r = 0.5\,R$.

If the temperature gradient remains constant for the total distance $R-r$, the temperature of the core would be approximately 100,000°C.

The most probable energy of thermal agitation of the atoms corresponding to the temperature of 100,000 would be equal to the energy an electron would have when accelerated by a potential of 15.0 volts, a potential much greater than the first ionization potential for all the elements forming the core. In fact, this potential is sufficient to remove the outer shell of electrons from all mono-, di- and trivalent atoms. Corresponding ionization will be produced by collision between atoms due to thermal agitation.

Although the probability of ionization by collision is very small, and the life of an excited atom very short the velocity of atoms at these high temperatures would be so great, and the mean free path at the high pressures existing in the interior of the earth so small that the number of collisions in 10^{-8} seconds, i.e., during the life of an ionized atom would be about 10^5, a number amply sufficient to produce ionization. The calculations are based on the assumption that the considerations of the Kinetic Theory of Gases may be applied to these temperatures and pressures.

When ionization results in the removal of the outer electron shell the radius of the ionized atom may be calculated from the Bohr Theory, assuming that the radii of successive shells are in the ratio of $1^2:2^2:3^2$:, etc. While this procedure often leads to wrong results,[6] it is by far the most reliable guide available. On this basis the average density of the ionized atoms is about ten times as great as that of the unionized ones. Where

the collisions at the assumed temperatures is not sufficient to remove the whole shell from some atoms of greater valence, they are sufficient to doubly and triply ionize the material.

No guiding principle exists which would enable one to calculate the radius of ionized atoms. Some work has been done on the size of ionized atoms in crystals,[7,8] which seems to indicate that the resulting radius of the atom is very much smaller than in the neutral state, but the considerations on which these calculations are based cannot be applied here. It is, however, reasonable to assume a great diminution in the space occupied, inasmuch as these collisions will result in the removal of the outer layer of electrons according to the Bohr Coster model of electronic arrangement. Under these conditions the density would easily reach a value of 15 gms./cc.

It is not necessary to have as high a temperature as 100,000°C. in order to produce these effects. It can easily be shown that a temperature of about 40,000° would be sufficient to produce the necessary ionization, if we take into consideration the Maxwellian distribution of velocities. The number of atoms which would have the energy of thermal agitation corresponding to 15–20 volts would be great enough and the number of collisions of other atoms with these frequent enough to produce the proper degree of ionization in the material of the core, especially if we take into consideration the relative velocities of the two atoms colliding.

Radioactive disintegrations may easily account for the high temperature of the interior. Lead and other products of radioactive disintegration form about 0.1% of the crust of the earth. If a similar abundance is assumed for the whole of the earth, and further it is assumed that only as little as one-tenth of this disintegration had taken place on this planet while the rest was taking place while the earth was a part of the sun the heat produced in the process of disintegration was sufficient to raise the temperature of the core to 100,000 degrees even if a specific heat of 3 is assumed for the liquid mass of the core, since the heat of disintegration is known to be about 10^9 calories/gm.

The theory outlined above accounts satisfactorily for the known mass and for the distribution of the mass inside the earth. The liquid core consequence of the theory is also in agreement with the known reflection of seismic waves from the interior of the earth. None of the assumptions on which this theory is based runs contrary to accepted facts. It must be mentioned on the other hand that too little is known concerning the properties of matter at very high temperatures and pressures, and the conclusions must, therefore, remain somewhat uncertain. However, the paper here presented has for its aim not a dogmatic explanation of the density of the earth, but rather is it an effort to call attention to a new, probably more satisfactory method of attack of the problem.

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[1] E. D. Williams and L. N. Adams, *J. Wash. Acad. Sci.*, **13**, 419, 1923.
[2] H. Jeffreys, *The Earth*, 2nd Edition, Chap. 12.
[3] Celia H. Paine, *Stellar Atmosphere*, Harvard Univ. Press, 1925.
[4] R. A. Millikan and C. Cameron, *Phys. Rev.*, **32**, 533, 1928.
[5] H. Jeffreys, *The Earth*, Chap. 8.
[6] J. H. Jeans, *Astronomy and Cosmogonoy*, 2nd Edition, Chap. 5.
[7] A. M. Berkenheim, *Zeit. f. Phys. Chem.*, **141A**, 35, 1929.
[8] L. Pauling, *Zeit. f. Krystallographie*, **67**, 379, 1928.

ROTATIONAL RAMAN SPECTRUM OF CO_2

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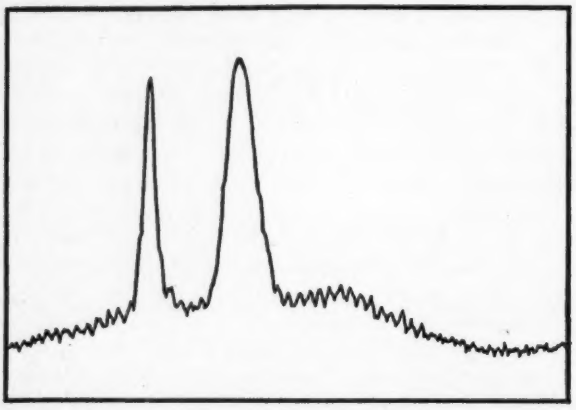
The Raman effect provides a convenient means of studying the rotation spectrum of many molecules, and avoids many of the difficulties inherent in work in the infra-red. The principal obstacle to rapid work is the low intensity of the scattered light. This may necessitate an inconveniently long exposure time, if a high dispersion spectrograph is used. However, by extending the methods first used by Rasetti,[1] we have been able to get good photographs of the oxygen rotation band in two hours.

The gas is contained in a quartz tube about 20 in. long and 1 in. inside diameter. The walls are $^1/_{16}$ in. thick and have withstood a pressure of 400 lbs. per sq. in. Although the increased pressure improves the intensity, it also broadens the lines to such an extent that the CO_2 rotation band cannot be resolved at pressures much above 75 lbs. per sq. in.

The exciting source is a water-cooled mercury arc in the form of a very narrow U. Its effective length is about 35 in. and it operates with 10 amp. The arc and the tube are enclosed in a chromium-plated cylindrical reflector which serves to conserve the light as well as to support the apparatus. A small dish of mercury is placed inside the Hilger E_1 spectrograph. This reduces the intensity of the scattered λ2536 exciting line to such an extent that it is nearly the same as its ordinarily weak companion, λ2534. Since the structure of the CO_2 band is almost at the limit of resolution of the spectrograph, it is necessary to control the temperature very carefully during the 10 or 12 hours of the exposure. For this purpose the spectrograph is enclosed in a box made of celotex, and the temperature of the room outside is maintained constant within half a degree by a thermostat.

Figure 1 is a tracing made from a microphotometer curve of one of the CO_2 plates. The rotation band appears to be composed of equidistant lines, with no evidence of the irregularities in spacing and intensity which would be produced by the presence of more than one moment of inertia.



The measured values of the wave-length changes are given in table 1. Since the position of the over-exposed exciting line is rather hard to de-

TABLE 1

m	J	SHIFT IN CM.$^{-1}$ OBS.	CALC.	OBS.
1	0	...	2.36	.....
2	2	...	5.51	.....
3	4	...	8.66	− 8.93
4	6	11.58	11.81	−11.67
5	8	14.76	14.96	−14.91
6	10	18.25	18.11	−18.02
7	12	21.59	21.26	−21.46
8	14	24.52	24.41	−24.67
9*	16	27.58	27.56	.....
10	18	30.66	30.71	−30.73
11	20	33.92	33.86	−33.29
12	22	37.08	37.01	−36.97
13	24	40.21	40.16	−40.23
14	26	43.42	43.31	−43.36
15	28	46.45	46.46	−46.52
16	30	49.84	49.61	−49.50
17	32	52.46	52.76	−53.46
18	34	55.54	55.91	.....

termine, the shifts are measured from a point half-way between the positively and negatively shifted lines. This differed by 0.36 cm.$^{-1}$ from the estimated position of the mercury line.

The calculated wave numbers are from the equation

$$\nu = (3.150/8)(4J + 6). \quad (1)$$

This formula, together with the values used for J, shows that the rotational quantum number, J, changes by two units in a transition, that only even rotational states are present, and that the moment of inertia is 70.2×10^{-40} g. cm.^{2} Since the positions of the lines are probably not more than 0.5 cm.$^{-1}$ in error, this value for the moment of inertia is probably correct within one or two per cent. The large difference between this value and the ordinarily accepted one due to Barker[2] may indicate that the rotation of the molecule is very considerably disturbed by its vibration. If this were true one might also expect that the moment of inertia would increase appreciably for values of J as high as 30. However, the measurements are not precise enough to make sure as to this point.

The uniqueness of the above interpretation of equation (1) is guaranteed by the fact that the position and the ordinal number n of the line nearest the intensity maximum can be determined. (The * in table 1 indicates this line.) Let a be the number of units by which J changes in a transition, and let δ be the number of units between one existing value of J and the next. Then

$$E_J = BhcJ(J + 1) \text{ and} \quad (2)$$

$$\Delta\nu = 2a\delta B \quad (3)$$

where ΔV is the wave number difference between two adjacent lines in the Raman spectrum. Also, from the relative population of the rotational states,

$$J^* = (n^* - 1)\delta + \alpha = (kT/2Bhc)^{1/2} - 1/2 \quad (4)$$

where n^* is the ordinal number of the strongest line, and α is the lowest value of J. Furthermore,

$$\nu^* = a\{(2BkT/hc)^{1/2} + aB\} \quad (5)$$

and

$$\nu_1 = aB\,(2\alpha + a + 1), \quad (6)$$

where ν_1 is the shift of the first line. From the last four equations the quantities a, δ, and α can be shown to lie nearest the integers 2, 2, and 0. With these values equation 3 gives B equal to (3.150/8).

[1] F. Rasetti, *Phys. Rev.*, **34**, 367, 1929.

[2] E. F. Barker, *Astrophys. J.*, **55**, 391, 1922.

B= .39325 cm^{-1}